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PYELITIS IN TOXEMIAS OF PREGNANCY

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IT IS becoming increasingly apparent that the term "toxemia of pregnancy" has little but tradition to recommend it and that the assumption which it implies is unjustifiable. No etiologic toxic products have yet been found by the most ardent advocates of the toxemia theory. There is increasing recognition of the fact that the syndromes encountered in the toxemias differ only in their incidence and speed of development from similar pathologic conditions that occur in nonpregnant women and in males. The question naturally arises whether the fundamental etiologic factors may not also be identical and whether pregnancy does not act only as the predisposing or precipitating cause for an acute explosion. One means of testing this theory is to analyze cases in which recognized renal or vascular diseases occur in conjunction with pregnancy. The most obvious condition of this kind is pyelitis.

MATERIAL AND RESULTS

For the purpose of this investigation, first of all, the records of all cases that received a diagnosis of toxemia of pregnancy in the New Haven Hospital from 1922 to 1935 inclusive, were collected and reviewed. To these were added 11 patients from the medical service of the hospital who had renal or vascular diseases that began during pregnancy. Finally the records were searched for patients with pyelitis during pregnancy who did not develop toxemia or receive the diagnosis "toxemia." Altogether there were between 350 and 400 cases in the first two

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groups, of which only 320 were accepted. The others were rejected either because their records were entirely inadequate or because they did not have toxemias of the type under consideration, but only severe vomiting of early pregnancy. The accepted cases are of uneven value because diagnostic procedures, therapy, and subsequent observations were not uniformly controlled by any one person with a specific purpose. A large number, however, were seen by the senior author or members of his staff, and many were followed for variable periods in the metabolism clinic.

Of the 320 cases, 41, or 13 per cent, suffered at one time or another from conditions generally included under the terms pyelitis or pyelonephritis. There is sufficient evidence in many other cases to indicate that the actual incidence of the condition was far greater; but only those cases about which there could be no uncertainty are included in this group. Abstracts of the protocols are presented at the end of the paper.

Among the 41 cases 11 came to autopsy, where the condition was verified. The first 12 protocols give the records of these cases, and of one other, A 32,601, who is added for reasons mentioned below. This represents 44 per cent of the 25 known toxemia patients on whom autopsies were made during the period covered by this report, strengthening the impression that the condition occurs more frequently than it is recognized. These autopsied cases provide a sounder basis for analysis than the others and will, therefore, be discussed first.

The first case, A 39,242, presented an extremely acute picture which seemed to originate during pregnancy and culminated in a rapidly fatal eclamptic syndrome during delivery. At autopsy acute bilateral pyelonephritis was discovered. Case 2, A 1,714, had toxemias in two successive pregnancies, the second typically eclamptic and fatal. Besides an acute bilateral pyelitis and ureteritis, she had a hydronephrosis with secondary changes in the kidney that can have been the result only of a longer-standing condition that may well have originated from her previous pregnancy toxemia. Case 3 (3,666) after two toxemias developed a fatal suppurative pyelitis and cystitis. At autopsy, besides the acute infection, a chronic hydronephrosis was found with secondary changes which indicated a disease of longer duration than that of the first two cases. Case 4 (63,494) beginning with an acute eclamptic seizure at the end of her first pregnancy, associated with pyuria, subsequently ran the usual course of chronic infected bilateral hydronephrosis, terminating fatally five years later. At autopsy extreme secondarily contracted pyelonephritic kidneys were discovered, together with the characteristic lesions in the general vasculature. Case 5 (44,154) is quite similar except that the disease ran a far longer course, altogether twenty-two years. It is quite probable that the abdominal pains of which she complained for so many of these years were all referable to the renal condition. Case 6 (A 9,526) had a comparable history, but was not seen during the original pyelitis. The same is true of Case 7 (8,250) moreover, in this case a congenital anomaly of the urinary tract may have played a contributory rôle. In Case 8 (31,841) pyelitis developed out of pregnancy, which seems merely to have aggravated the condition. A congenital anomaly which caused obstruction of the lower urinary tract undoubtedly acted as a predisposing cause for the pathologic lesions found in Case 9 (47,162) who had a typical eclamptic toxemia. Case 10 (29,869) is included in the autopsy category; however, the autopsy was performed at another hospital, where she died, and contributes little because the report is so inadequate. In Case 11 (53,431) the patient died from adventitious causes five years after the initial toxemia, had no pyelitis or pyelonephritis at autopsy, but did exhibit signs of permanent injury from previous disease in dilatation of the right renal pelvis and ureter. Case 12 (A 32,601) has not been included in the roll of pyelitic subjects. The immediate cause of her death was bronchopneumonia. In addition she had pathologic lesions in liver and kidney which

are usually connected with eclampsia.   The dilatation of the right ureter and renal pelvis, unaccompanied by infection of the urinary tract, are probably only part of the changes found in normal pregnancy.

The next seven patients died, but did not come to autopsy.   Among these pyelitis or hydronephrosis, or both, were demonstrated by cystoscopic examination at some time in four, Cases 13, 16, 17 and 18 (37,453, 20,921, 55,527, and 15,177).   In the others the diagnoses were made from symptoms and urinary findings only.   In four, Cases 16, 17, 18 and 19 (20,921, 55,527, 15,177, 23,706) death occurred long after the original pyelitis, which seems to have originated during a toxemic pregnancy in 15,177 and 23,706 and in the other two to have preceded the pregnancies in which toxemias appeared.   These cases resemble in all respects those of the autopsy series who had secondarily contracted pyelitic kidneys.   One of those who had pyelitis preceding her toxemic pregnancy, Case 17 (55,527) had a typical eclamptic syndrome.   The remaining three, Cases 13, 14, 15 (37,453, 35,348 and A 9,052) died of fulminating toxemias.   The first had eclampsia; the second died three weeks after delivery; the course of the third resembled closely that of Case 2 (A 1,714) of the autopsy series.   Only Case 13 (37,453) is known to have had pyelitis before the onset of her toxemic pregnancy, and this originated in an earlier pregnancy that was terminated.

The remaining 23 comprise an extremely miscellaneous group of cases.   The diagnosis in 13, Cases 20 to 32 (53,658 to 26,573 inclusive) was established by means of the cystoscope or intravenous pyelography, in the remainder by symptoms, signs, and urinary findings.   There are three instances of eclampsia: one in Case 20 (53,658) with pyelitis which arose during pregnancy and, in spite of treatment before and after delivery, left permanent and irreparable marks in the urinary tract; one in Case 41 (81,771) who, twenty-five years later, had the hypertension and associated signs of vascular disease that mark the advanced stages of chronic contracted hydronephrotic kidneys; the third in Case 33 (70,951) who had an unmistakable pyelitis although the diagnosis was not established by cystoscope or pyelograms.   The fate of this patient is not known.   The other 12 who had cystoscopies exhibited toxemias of every variety and of every degree of severity.   In fact some of the syndromes were so mild as hardly to deserve the appellation of toxemia.

Of the remaining cases, in which the diagnosis was not established by direct examination of the urinary tract, but little need be said.   These examinations were not made, usually because the urinary infection was relatively slight or because the period of observation was short.   It is natural to find in this group the least severe cases.   Nevertheless, the ultimate severity cannot be predicted from the character of the symptoms in the initial stages of the disease, as the records of some of the cases in the earlier groups testify.

DISCUSSION

It has now been established that in the majority of normal women in the latter part of pregnancy, the pelves of the kidneys and the ureters above the pelvic brim are dilated, owing to some obstruction of the intrapelvic portions of the ureters.[1-9]   Whether this condition results from compression by the gravid uterus or from hyperplastic changes in the pelvic portions of the ureters is of little importance for the present argument.   The right ureter is more frequently and more seriously affected.   It has been clearly recognized that this condition subjects the pregnant woman to greater risk from pyelitis,[2, 10-16] increases the dangers of pyelitis and militates against its effective treatment.   The tendency for pyelitis to become chronic and to recur in

future pregnancies has been noted by Kretschmer,[15] Crabtree and Prather[16] and others. The relation of these anatomical distortions and infections of the urinary tract to toxemias has, however, received little emphasis, or else it has been too generally assumed that these toxemias differ from those which are not accompanied by pyelitis or pyelonephritis.

Wüllenweber[18] made the suggestion that pressure in the renal pelvis during pregnancy, by impairing kidney function, gave rise to the toxemias. This hypothesis can hardly be accepted in view of the now recognized frequency of hydronephrosis and increased ureteral pressure. Some additional factor must be hypothecated. Williams[13] and Hunner[14] in calling attention to the seriousness of pyelitis in pregnancy cite each one case that developed symptoms or signs of toxemia, but the significance of these in relation to the pyelitis either escaped attention or was not especially emphasized. In most of the other reports cited above attention was confined to urologic aspects of the disease to the exclusion of general systemic manifestations or functional disturbances. Rockwood, Mussey and Keith,[19] after reviewing 100 consecutive cases of toxemia, concluded that they conformed in general with renal and vascular diseases encountered in nonpregnant subjects, according to the classification of Volhard and Fahr. In this classification pyelitis and pyelonephritis form one category to which Rockwood, Mussey and Keith consigned 34 out of the 100 cases. None of these is described in the report, but under the heading of acute nephritis appears a patient whose history is marked by pains in the back and abdomen and pyuria who proved at death, after recurrent toxemias, to have bilateral infected hydronephrosis. Because this subject presented initially edema, hypertension, and other signs of toxemia, the pyelonephritis is looked upon as a complication of an acute nephritis. Kahn,[20] largely on the basis of bacteriologic studies of the urine, with more extensive examination in certain cases, found some evidences of pyelitis in 40 out of 52 cases of toxemia which he examined. Hirst[21] suggested that there was some relation between anatomic obstruction and infection of the urinary tract and the late toxemias of pregnancy. O'Sullivan[22] in a discussion of "albuminuria in pregnancy" recognizes two major classes, those without and those with bacilluria. Of 67 cases, 46 belonged to the latter group and of these 10 had hypertension. He calls attention to the fact that pain, dysuria, and other symptoms of urinary tract infection may be absent, and blood chemistry and functional tests may be normal in these cases. Edema was frequent. The course was often afebrile until the puerperium; but after delivery fever was the rule, whereas it was rare in patients without bacilluria. In both classes respiratory infections frequently preceded the onset of toxemia. Evans,[23] in a follow-up study found that 4 out of 76 patients with noneclamptic toxemias, after intervals of from four months to four years had definite cystitis or pyelitis. McIlwraith[24] recognizes infective nephritis with positive urine cultures as one of the causes of eclamptic or preeclamptic toxemias. Bell,[25] in 10 autopsies of patients who died from eclampsia, found the right ureter dilated 3 times, the bladder twice, and the left ureter once. This, in itself, means little. Since some degree of hydronephrosis is so commonly a part of pregnancy, it is only surprising that he did not find it more often.

This does not pretend to be an exhaustive review of the voluminous literature on the urinary disorders of pregnancy, but is believed to be fairly representative of opinions on the subject, especially in relation to toxemias. Throughout there is a striking tendency to separate pyelitis of pregnancy from other toxemias, apparently chiefly because

it has a more definite pathogenesis. This exhibits itself in a general tolerance to more conservative treatment, which is strangely (inconsonant) with the repeated confession that pyelitis, even without toxemic complications, if it extends into the latter months of pregnancy, when ureteral obstruction is established, is extremely refractory to treatment, can seldom be cured before delivery, leaves permanent anatomical residua, and is likely to recur in a more aggravated form in subsequent pregnancies.

In relation to the course of disease the cases here reported can be divided into four classes: (1) Those who developed pyelitis before the particular pregnancy in which toxemia occurred; (2) those who developed pyelitis early in pregnancy; (3) those in whom pyelitis was discovered during the puerperium; (4) a small number who had antecedent toxemias and later developed, or were found to have, pyelitis. The relation to toxemias of the pyelitis and pyelonephritis in the last two classes is especially open to question. In many, if not most, of the cases in which pyelitis was not discovered until the puerperium, it is not improbable that it had preceded labor without having been recognized. This was evidently the order of events in Cases 3 and 2 (3,666 and A 1,714), as the postmortem findings testify. In the latter there is good reason to believe that hydronephrosis attended a preceding toxemic pregnancy in which no symptoms of pyelitis were recognized. It is not possible to secure equally good evidence in the cases of Class 4 who did not come to autopsy.

Of the 41 patients, 25 had outspoken toxemias, 9 with eclamptic seizures. Four had hypertension or edema or both. One had pregnancy terminated early. The remaining 11 either were not seen in their initial illnesses or else were delivered elsewhere. In these the diagnosis of toxemia depends on anamnesis or the subsequent clinical course. Almost all received a diagnosis of toxemia of one kind or another. To maintain that in the most authentic cases the coexistence of pyelitis and toxemia was only coincidental would be less than openminded so long as the true cause and nature of toxemias are still unknown.

It is relevant to inquire why, if toxemias so commonly result from pyelitis, the fact has not long since commanded more recognition from urologists as well as obstetricians. It seemed profitable, therefore, to search the records of the hospital for cases of pyelitis occurring in the course of pregnancy in which the diagnosis of toxemia was not made. It was found that out of 93 such cases, 25 developed before term definite hypertension (systolic pressure 150 or over; diastolic 90 or over), sometimes accompanied by edema. The number would probably have been larger if more assiduous attention had been given to examination of blood pressure. Considering that the records examined include subjects who had pyelitis which subsided in the early months of preg-

nancy, and others who could not be observed throughout pregnancy, the proportion who developed signs suggesting toxemia is by no means insignificant. If these 25 patients are included among the pyelitic toxemias the number of these is swelled to 66, or 19 per cent of all the toxemias. In addition to those who developed hypertension and edema, there is a large group of patients who, after pyelitis of pregnancy proved to have permanent anatomical injuries of the urinary tract, hydronephrosis, ureteral strictures, etc.

If a relation between pyelitis and toxemias is admitted, current concepts concerning the etiology and pathogenesis of the latter are hardly tenable. Nine of the patients in this series had typical attacks of eclampsia. In many of these the existence of pyelitis had been established in advance of the toxemia, in some it had long preceded the toxemia. In this connection the patient, Case 9 (47,162) in the autopsy group, is particularly illuminating because she had a congenital lesion of the urinary tract which had evidenced itself in hyposthenuria and albuminuria long before her first pregnancy. Instead of eclampsia, then, she should have presented the pictures which are described under the terms, "low reserve kidney" or "nephritis of pregnancy." To claim that the seizures which these patients had were not truly eclamptic implies a preconception about the nature of this type of toxemia for which there is no warrant. After all, the only features by which it can be distinguished are its sudden onset and the convulsive explosions, which are beautifully illustrated in such cases as 1, 13, 20, and 33 (A 39,242, 37,453, 53,658, and 70,951). Too much emphasis must not, however, be placed upon the association between pyelitis and eclampsia. Almost every clinical syndrome described among toxemias is illustrated by one or other of the cases which have been described. This is not surprising if it is appreciated that quite similar incidents may occur in the course of chronic pyelitis, hydronephrosis, and pyelonephritis without pregnancy. For example, in this series Cases 16, 17, and 8 (20,921, 55,527 and 31,841) had convulsive seizures subsequent to their toxemias, while the patients were neither pregnant nor in the terminal stages of their disease. This lends support to the earlier suggestion that the rôle of pregnancy in the etiology of toxemias may be merely to accelerate or exaggerate the progress of a pathologic condition which is of itself capable of producing a similar picture in the nonpregnant subject, evoking an acute explosion or exacerbation of the disease.

To deny the toxemic character of these cases entirely becomes an idle gesture in view of the fact that the great majority initially received the diagnosis of toxemia. Nor can this be ascribed to any peculiar local ignorance or negligence, since the records show that in many instances the original diagnosis of toxemia was made elsewhere, while the true condition was discovered here. The term toxemia may ill fit patients with pyelitis and pyelonephritis of pregnancy, but

it cannot be denied them without a redefinition of toxemia so radical that it would demand a complete revolution in the philosophic attitude toward these interesting complications of pregnancy, and would probably end in abolishing the term toxemia and all that it implies. However beneficial such a revision might be for the future, it cannot serve as a basis for retroactive criticism. The term "toxemia" has been applied broadly to certain symptoms occurring singly or in more or less characteristic complexes in the course of pregnancy, the chief of which are albuminuria, hypertension, edema, and convulsive seizures. These cases of pyelitis without exception exhibited one and usually more of these symptoms.

The postmortem pathology of the autopsied cases has not been described or discussed in detail, partly for lack of space, chiefly because this aspect of the subject will be discussed in a separate communication, dealing with the pathology of toxemias of pregnancy as a whole. To those who look upon morbid anatomy as the ultimate criterion for the differentiation of toxemias, it may be said that the patients who died in the acute stages of the disease presented, in addition to pyelonephritis, the tubular and glomerular changes which are considered characteristic of eclampsia, and in addition sometimes hemorrhagic and necrotic lesions of the liver. Lest it be claimed that these cases were probably exceptional instances in which pyelonephritis and eclampsia occurred coincidentally, we hasten to add that in the subsequent discussion of the pathology of toxemias, we hope to demonstrate that these lesions are characteristic of no particular type of toxemia and bear no clear relation to the details of the clinical syndrome nor to any antecedent pathologic condition which may have acted as a predisposing cause.

The failure to recognize the rôle of pyelitis earlier with more frequency may be attributed to the fact that it does not always manifest itself by the traditional signs and symptoms. Pain and lower urinary irritation may be almost or entirely lacking, although they appeared in this series more often than their significance was recognized. Experience gives the impression that they are especially likely to be inconspicuous in persons who have obstructive lesions of the urinary tract. This is exemplified by the autopsied Case 9 (47,162), and by other patients with congenital obstructive lesions in our own case records and in the recent reports of Longcope[26] and Ellis.[27] Just such an obstructive condition is provided by the well-recognized hydronephrosis of pregnancy, whether this be ascribed to pressure by the pregnant uterus or to morphologic changes in the walls of the ureters. Something more than the usual perfunctory prenatal examinations of urine and blood pressure is essential, if pyelitis is not to be overlooked. At the very least microscopic examination of a clean voided specimen as well as the routine test for albumin is indicated. Albuminuria, except in the most acute phases, may be inconspicuous, and

blood pressure may not rise until the toxemic explosion. More weight must be given to complaints of pain in the abdomen or back, urinary frequency and burning, and other subjective complaints that are too lightly attributed to irritability arising from the natural discomforts of pregnancy.

The seriousness of the association of pyelitis and pregnancy, if these protocols are typical, little justifies the casual attitude which it is usually accorded. The present series of cases represents a formidable group and includes subjects who received all the benefits of the most modern methods of treatment, although this phase of the subject has not been stressed in this report. It has long been clearly recognized that elimination of urinary infection in the presence of obstruction of the urinary tract is difficult, if not impossible. There is no reason to believe that in this respect a physiologic obstruction is more benign than a pathologic one.

Of the 41 cases presented, 7 died in the acute stages of toxemias; 10 after long and miserable illnesses, with secondarily contracted pyelitic kidneys. One, who died of adventitious causes, proved to have chronic hydronephrosis. Another 7, unless they have succumbed, are living with residua of the disease which will inevitably bring them to the same end. Six, after intervals of one to eight years, have symptoms or signs that suggest that they belong in the same class. Nine have been followed for such short periods or disappeared so early that it is impossible to predict their fate. On the basis of past experience it may be reasonably expected that a certain proportion of them will return to spend their last days of misery in the hands of the medical service. Only Case 24 (81,853) seems with any certainty to have escaped serious consequences; her pregnancy was terminated quite early, before any toxemic symptoms had developed, on the basis of the pyelitis alone.

One of the outstanding characteristics of pyelonephritis is its insidious progress and long duration. The duration of life after pyelitis became established in those of this series in which it can be accurately established was: Cases 4 (63,494), five years; 5 (44,154), twenty-three years; 6 (A 9,526), nineteen years; 7 (8,250), seventeen years; 8 (31,841), sixteen years; 9 (47,162), thirteen years; 16 (20,921), twelve years; 17 (55,527), seven years; 18 (15,177), six years; 19 (23,706), eighteen years; 30 (7,841), more than ten years, at least; 31 (34,922), over twenty-five years; 32 (26,573), over twelve years; 37 (35,865), at least four years; 41 (81,771), over twenty-five years. In contrast the term of happiness and health is pitifully short. Death usually comes after a long and lingering illness in which hypertension and its sequelae are much more in evidence than renal insufficiency. In fact it is notorious that a large proportion of these cases are mistaken for benign or malignant nephrosclerosis. The onset of hypertension is capricious in the extreme and for long periods the blood pressure may be so variable as to give the impression of a functional vasomotor disturbance. The urine much of the time seems relatively innocent, containing little or no albumin and only occasional white blood cells.

The course of the disease is, however, usually punctuated by recurrences or recrudescences of infection in which pyuria appears and hypertension and its associated evils advance.

Such advances are usually determined by the intervention of another pregnancy, in which toxemic symptoms frequently recur. Subsequent toxemias occurred in at least 10, probably 13, of the reported cases, a large proportion in view of the number who died of acute toxemias, those who had no subsequent pregnancies, those who were lost to view and those who have not yet had time to become pregnant again. In two cases the recurrences were frankly eclamptic, in both instances in patients who had originally eclampsia. It is frequently stated in the histories that subsequent pregnancies were uncomplicated. Such statements cannot be taken at their face value in view of the fact that, when objective examinations are available in similar cases, signs of toxemia are frequently observed. Nevertheless in individual pregnancies certain persons appear to escape unscathed. The factors which determine recurrence of toxemia remain to be discovered. There are vague suggestions in some of the protocols that the secondary disasters depend upon reinfection. The usual criteria of recovery, restoration of normal blood pressure and elimination of pyuria and albuminuria appear to be quite inadequate. Normal urine and blood pressure have been demonstrated in patients who have demonstrable hydronephrosis and in subjects in the advanced stage of the disease. Even renal functional tests fail to reveal the nature of the disorder until it has reached an advanced stage. Certainly the restoration of normal blood pressure and urine gives no insurance against a recurrence with subsequent pregnancies.

In the one patient who appears with reasonable certainty to have escaped sequelae or residua (Case 24, 81,853), pregnancy was terminated early for pyelitis alone, before toxemic symptoms had developed. Similar treatment in the other cases might not only have prevented untold suffering and untimely deaths; it might also, by enabling these women to rid themselves of their infections, have contributed ultimately more and better offspring. As is the case in all toxemias, the rôle of viable healthy children in behalf of which these pregnancies were allowed to continue is distressingly small. It is not only imperative that pyelitis of pregnancy be earlier and more frequently recognized, but that it be considered an indication for the termination of pregnancy. With the physiologic obstruction removed, continuous natural drainage is more likely to effect a cure than temporary or intermittent drainage secured by posture or instrumentation. And there may be hope that if the primary disease is cured it will not recur in subsequent pregnancies.

It is not intended to give the impression that pyelitis is or even may be the direct or remote cause of all pregnancy toxemias. It is believed that the present report underestimates its actual importance in the

production of these conditions. It is presumably, however, only one of a group of renal and vascular disorders which may serve this purpose. The reasons for this view will be presented in subsequent communications. Pyelitis has been selected for first consideration, because it is the most obvious of these disorders and can be demonstrated in the most unequivocal objective manner.

SUMMARY

Of 320 patients with toxemias of pregnancy, 41 were found to have pyelitis.

Of 25 autopsied patients with vascular or renal disease that first manifested itself in pregnancy, 11 were found to have pyelitis and hydronephrosis or their sequelae.

Of 93 patients with pyelitis complicating pregnancy, 25 developed, before pregnancy was terminated, hypertension or edema or both.

Reasons are given for believing that pyelitis in these patients was a major etiologic factor in the production of toxemia.

INDIVIDUAL CASE RECORDS

CASE 1.—Primipara, born 1911, entered hospital at term, Apr. 24, 1934. Extreme frequency and occasional pain after micturition, since onset of pregnancy; occasional dizzy spells and increasing edema for one month. B. P. 174/104, edema up to the knees. Insertion Voorhees' bag 7:30 P.M.; several convulsions beginning at 8 P.M. Death from circulatory and respiratory failure at 9 P.M. just after delivery of dead child by version and extraction.

Autopsy: Bilateral hydroureters and hydronephrosis; acute bilateral pyelitis; polynuclear infiltration of kidneys, especially near the pelvis; extensive necrosis of renal tubules.

CASE 2.—Born 1907. 1929, delivery at home after 7 weeks in bed with edema and hypertension. About June 1, 1931, in last month of pregnancy, edema of feet, extreme urinary frequency and burning. June 11, abdominal pain, followed by vomiting and later convulsions. Admitted to hospital comatose, with stertorous breathing, moderate edema of extremities, enlarged liver, jaundice, B. P. 182/130. Blood pressure fell rapidly, shock developed, with death in a few hours, temperature rising to 102.2°. Catheterized urine grossly bloody, with much albumin and many casts. N.P.N. 41.

Autopsy: Bilateral hydroureters and hydronephrosis with pyelitis, necrosis of renal tubules, acute hemorrhagic hepatitis. Hydronephrosis evidently of long standing, antedating immediate illness.

CASE 3.—Born 1898. Normal delivery 1917; delivery at 8 months for toxemia in 1919 with postpartum fever ascribed to puerperal infection; miscarriage at 5 months in July, 1921, after development of edema. After this exacerbation of long-standing ''indigestion'' (abdominal pain). About Nov. 1 sudden chill, acute dyspnea and orthopnea and severe headache, followed next day by persistent vomiting, muscular cramps, precordial and lumbar pain. (Illness was preceded by ''cold in chest'' with cough.) Later developed epistaxes, dizziness and blurred vision. Entered hospital Nov. 22, B. P. 170/120, retinal edema and hemorrhages, râles and friction rub over left chest, abdominal tenderness, fever, albuminuria, pyuria, profound anemia, leucocytosis, N.P.N. 171. Died Nov. 29 with cardiac and renal failure and terminal parotitis.

Autopsy: Chronic cystitis, bilateral hydronephrosis, chronic ureteritis and pyelitis, acute suppurative cystitis and pyelitis. Postmortem blood culture hemolytic streptococci.

CASE 4.—Born 1905. Entered hospital Mar. 18, 1928, for convulsions two days after birth of 7.5 months' fetus. Stuporous, temperature 101.4°, B. P. 186/117, slight edema of face, ankles and retinae, pus, hemolytic streptococci and colon bacilli in catheterized urine, N.P.N. 69. Puerperium febrile. Relapse with fever, headache, and lumbar pain after discharge. May 29, B. P. 160/120. Pleurisy after miscarriage in 1930, led to discovery of hypertension and renal disease. Nov., 1932, after respiratory infection, headache, and bilateral costovertebral pain, diurnal and nocturnal urinary frequency. Feb., 1933, increasing vomiting. Entered hospital Apr. 27, B. P. 170/95, retinal arteriosclerosis, heart failure, albuminuria and pyuria, N.P.N. 181. Persistent vomiting, steady deterioration to death June 1. Convulsion Apr. 30.

Autopsy: Bilateral hydronephrosis and hydroureters, chronic and acute ureteritis and pyelitis, extreme contracted kidneys.

CASE 5.—Born 1889. In seventh month of pregnancy, 1912, chills, vomiting, pain in legs and back, urinary frequency and urgency, hematuria. After this pains and tenderness on one or other side of abdomen or in back. In addition, after 1921, precordial oppression and anginal pain. B. P. 1921, 120/70; 1924, 160/90. 1930, hematuria and pain in both kidney regions. Supravaginal hysterectomy, left oophorectomy, salpingectomy, and appendectomy without relief. 1930, hematuria and bilateral renal pain. 1931, dyspnea, headaches, dizziness, increased urinary frequency, B. P. 265/140, tenderness in right hypochondrium and both lower quadrants, much albumin and few leucocytes in urine, N.P.N. 33. Steady deterioration of cardiac and renal function, with recurrent abdominal and lumbar pain, until death in 1935.

Autopsy: Dilatation of ureters and renal pelves, acute and chronic pyelonephritis, extreme contracted kidneys.

CASE 6.—Born 1892. "Pus on kidneys" in first pregnancy, 1913. Subsequent 3 pregnancies supposedly uncomplicated. 1926, pains in lower quadrants of abdomen. After 1930 increasing headaches and urinary frequency. Nov., 1931, dyspnea, followed later by increasing vomiting, paroxysmal orthopnea and substernal pain. Jan. 10, 1932, developed "grippe," Jan. 17, edema of feet and ankles. Entered hospital Feb. 14 with dyspnea, orthopnea, constant vomiting, anemia, signs of heart failure, B. P. 240/140, retinal scars and hemorrhages, edema of legs and sacrum, tenderness in right lower quadrant, urine of low specific gravity, with albumin, red blood cells, few leucocytes and casts, N.P.N. 198.

Autopsy: Dilatation of ureters and renal pelves, extreme contracted kidneys, acute suppurative pyelonephritis.

CASE 7.—Born 1886. "Kidney trouble" after first pregnancy, 1910. Subsequent attacks of urinary frequency and burning, lasting ten to twenty days, 4 or 5 times a year, with aggravated symptoms during pregnancies in 1914, 1918, and 1920. In eighth month of pregnancy, 1922, edema of ankles, albumin, leucocytes, epithelial cells and casts in urine, without hypertension. Urinary symptoms further aggravated in this pregnancy and another in 1924. Oct. 20, 1926, pain in back, urinary frequency and burning, dizziness, headaches, morning nausea, edema of ankles, B. P. 200/116. Feb. 10, 1927, albumin and leucocytes in urine, B. P. 216/135. Entered hospital Feb. 14 with phenobarbital poisoning (exfoliative dermatitis). Died Mar. 3.

Autopsy: General epithelial desquamation with terminal bronchitis and bronchopneumonia. Bilateral double ureters. Chronic and acute pyelitis with various degrees of dilatation of all four ureters and pelves and extreme secondary contraction of kidneys.

CASE 8.—Born 1894. First pregnancy ended in miscarriage at 6 months; second and third reported uncomplicated. 1916, backache, headache, hematuria, urinary frequency and burning. After this similar attacks at intervals, not relieved by appendectomy and uterine fixation in 1918. Exacerbation of urinary symptoms, dyspnea and blurred vision during pregnancy in 1924. Delivered in March. June 27, B. P. 130/82, symptoms persistent. 1925, edema late in pregnancy. Sept. 27, 1930, B. P. 220/120, albumin, pus, and blood in urine. December, cystoscopy revealed cystitis, bilateral pyelitis, distortion of pelves and calyces of both kidneys, moderate left hydronephrosis, calcareous shadows on right side. Attacks of severe renal pain, frequency, hematuria and increasing signs of heart failure until death, Jan. 26, 1932.

Autopsy: Cystitis, bilateral pyelitis with secondarily contracted pyelonephritic kidneys, right nephrolithiasis.

CASE 9.—Born 1901. Morning nausea and vomiting since childhood. During scarlet fever, 1919, low specific gravity urine with minimal albumin. 1920, vomiting 4 or 5 times a day throughout pregnancy. 1922, dyspnea, choking sensations and nervousness. 1925, hypertension, profuse albuminuria and pyuria discovered. 1927, convulsions after premature delivery. 1928 and 1929, occasional attacks of hematuria with convulsions. Early 1932, severe anemia, frequent epistaxes. Jan., 1933, "grippe" followed by persistent cough and extreme weakness. Entered hospital Feb. 16, semistuporous, dehydrated from vomiting, B. P. 165/94, albuminuric retinitis, enlarged heart, profound anemia, albuminuria and pyuria, N.P.N. 198. Death one month later.

Autopsy: Congenital hypoplasia of urethra and right kidney, bilateral hydroureters and hydronephrosis, chronic cystitis, ureteritis and pyelitis with suppurative pyelonephritis on left.

CASE 10.—Born 1901. Two normal deliveries, the second Jan., 1924. Early in March tonsillitis. Mar. 28, right lumbar pain, urinary frequency and burning, hematuria. Entered hospital Apr. 7, B. P. 119/70, both kidneys palpable, tenderness in right flank, temperature 103°, leucocytosis, albumin, pus and streptococci in urine. Cystoscopy Apr. 9 reported negative. June 26, 1925, early in pregnancy, albumin, few leucocytes and few red blood cells in urine, B. P. 94/44. Delivered elsewhere. Entered hospital Oct. 21, 1927, in early pregnancy, vomiting, with slight fever, little albumin, few leucocytes and casts in urine, B. P. 110/60. Entered another hospital Dec. 1, vomiting persisting, with difficulty in voiding, burning on urination, profound anemia, B. P. 115/78, albumin, rare casts and many leucocytes in urine. Death Dec. 3. Autopsy records secured from hospital inadequate.

CASE 11.—Born 1892. May, 1929, early in fifth pregnancy, nausea, vomiting and chills. Comparatively well July and August. Sept 9, pain in back and epigastrium, extreme urinary frequency, edema of feet and face. Sept 23, epigastric and right lumbar tenderness, edema of feet, albumin, occasional leucocytes and rare casts in urine. Pregnancy terminated Sept. 25. Puerperium febrile, complicated by femoral thrombophlebitis, pulmonary embolism, persistent pyuria and bacilluria. 1933, urinary frequency and burning. Cytoscopy May 17, 1934, bifid ureters, right hydronephrosis, N.P.N. 23, phthalein excretion 40. Death few days later from pulmonary embolus following uterine suspension.

Autopsy: Pulmonary embolus. Acute focal necrosis of renal tubules, hemorrhages and congestion of kidneys, some chronic glomerular lesions. Dilatation of right ureter and renal pelvis without pyelitis.

CASE 12.—Born 1896. Normal pregnancies 1925 and 1928, miscarriage 1931. Entered hospital 4 A.M. Dec. 20, almost at term, after 2 months' headache and edema of feet. Pulse 120, B. P. 160/110, edema of trunk and legs, slight cough.

8 A.M. cough worse, sputum bloody, breathing rapid, skin clammy, pulse 144. Signs of bilateral bronchopneumonia at 11 A.M. Death next morning. Albumin, leucocytes and red blood cells in urine, secondary anemia, leucocytosis.

Autopsy: Diffuse bronchopneumonia, extensive hepatic necrosis with inflammatory lesions, slight degenerative changes in renal tubules and glomeruli, dilatation right renal pelvis and ureter without pyelitis.

CASE 13.—Born 1892. First pregnancy terminated at 6 months early in 1924 for severe pyelitis. Later in same year, early in pregnancy, recurrence, treated conservatively. July 6, 1925, slight edema of feet. July 10, epigastric pain and nausea in A.M. Found in coma (presumably postconvulsive) at 4 P.M. Entered hospital, 9 P.M. after 2 more convulsions, with temperature 105°, B. P. 180/100. Blood pressure fell to shock levels after further convulsions. Delivery dead fetus July 7; death July 8, with terminal temperature 107.4°. Much albumin, many leucocytes, red blood cells and bacilli and occasional casts in 2 catheter urine specimens.

CASE 14.—Born 1902. Cesarean section at term for dystocia, 1924: albumin and many leucocytes in urine, blood pressure normal, course afebrile. Cesarean 1926; urine as before, B. P. 138/100, right costovertebral pain and pyuria during puerium. Entered hospital Oct. 11, 1927, with albuminuria, pyuria, edema, retinal edema, bilateral costovertebral tenderness, without hypertension, having had chills, fever and urinary frequency for some time. After cesarean section and section of fallopian tubes, Oct. 21, fever, increasing edema and hypertension. Nov. 13, convulsions, followed by coma and death.

CASE 15.—Born 1897. Pregnancy, 1925, presumably uncomplicated. Early in Dec., 1932, in seventh or eighth month, sore throat, hoarseness and cough, with later increasing nausea, vomiting, and epigastric pain. Entered hospital Jan. 2, 1933, vomiting, dehydrated, afebrile, with slight cervical adenitis, minimal icterus and edema, B. P. 130/90, extensive retinitis, many leucocytes and bacilli, but little albumin and rare casts in urine. Cesarean section Jan. 17. Death Jan. 27, preceded by fever, increasing to 104°, and terminally by nystagmus, strabismus, signs of tetany, left facial weakness and convulsions, but no hypertension.

CASE 16.—Born 1889. 1914, pyelitis. Recurrence 1918 and 1920, when cystoscopy confirmed diagnosis (bilateral), B. P. 118/70, phthalein excretion 78. 1922, after delivery, hematuria, fever and lumbar pain. Feb., 1925, dizziness, blurred vision, vomiting, weakness, fever and extreme urinary frequency. Entered hospital Mar. 1 after 2 convulsions, B. P. 200/150, advanced retinitis, albumin, casts and pus in urine, N.P.N. 53. Increasing renal and cardiac failure until death, June 8, 1926.

CASE 17.—Born 1888. Oct. 5, 1926, delivered at term after a week of hypertension without albuminuria. Oct. 6, sudden convulsion followed by sudden passage of large volume of urine. B. P. 230/160. Puerperium febrile, with persistent hypertension, urinary frequency and burning and profuse pyuria. History of cystitis preceding pregnancy. Cystoscopy Mar., 1927, cystitis and right pyelitis. Symptoms of urinary infection and hypertension until death from cerebral accident Mar. 29, 1933.

CASE 18.—Born 1892. Dec. 24, 1922, 4 months before term in third pregnancy entered hospital for hemorrhage from separated placenta, with albuminuria, cylindruria and B. P. 168/122. Pregnancy terminated. Puerperium febrile, hypertension persistent. Entered hospital Sept. 12, 1923, 3 months before term, with lumbar pain, headache, B. P. 250/150, retinal edema and cardiac enlargement. Supravaginal hysterectomy. Puerperium febrile. Hypertension, pyuria and pains in back persisted. 1927, hemiplegia. Bilateral hydronephrosis and pyelitis proved by cystoscopy. Death June 1, 1928, from intraventricular hemorrhage.

CASE 19.—Born 1887. 1907, in third month of first pregnancy, albuminuria and edema. Ill for a month following termination of pregnancy. 1914, entered hospital for similar condition. Aug. 29, 1923, in eighth month B. P. 154/94; Sept. 14, 160/100, albuminuria and pyuria. After delivery, Sept. 20, persistent hypertension and pyuria with pain in back. Oct., 1925, swelling of face, pallor and epistaxis, succeeded in December by dyspnea, nausea and vomiting. Entered hospital Dec. 17 *in extremis* with advanced renal and cardiac failure and died Dec. 19. N.P.N. 410.

CASE 20.—Born 1895. 1925, miscarriage. Burning urination 1 week in succeeding summer. Mar. 9, 1926, in third month, symptoms of pyelitis. April 14, cystoscopy revealed pus from left ureter, dilatation of left renal pelvis and impaired function of both kidneys. Treatment by renal lavage until July 29. Sept. 25, B. P. 150/90, rising to 172/90. Entered hospital Oct. 9, 3 P.M., vomiting, 6 P.M. convulsions, delivery 10:30. Puerperium febrile. Hypertension subsided. Cystoscopy, Mar., 1927, persistent left hydronephrosis, impaired function right kidney, unimproved by cystoscopic treatments and plastic operation on left renal pelvis.

CASE 21.—Born 1903. Entered hospital Oct. 15, 1935, at term. Symptoms of pyelitis early in pregnancy, febrile illness in August, edema leading to discovery of pyuria in September, followed by increasing hypertension and albuminuria. Oct. 18, cesarean section, followed by prolonged fever, renal pain and urinary frequency and burning, complicated by pleurisy with effusion. Nov. 7, intravenous pyelograms revealed right hydronephrosis and hydroureter. Pyuria persisted 2 months later.

CASE 22.—Born 1900. Entered hospital Jan. 7, 1928, 6 months pregnant with bilateral pyelitis, hydronephrosis and hydroureters (cystoscopic diagnosis), N.P.N. 43, phthalein excretion 50. Discharged and delivered at home. Readmitted Aug. 13, 1929, 3 months pregnant, with symptoms and signs of pyelitis and history of intermittent hematuria since previous pregnancy, B. P. 100/60. Pregnancy terminated by hysterectomy. Treatment in urologic clinic until Apr., 1932.

CASE 23.—Born 1899. Nov., 1920, in first pregnancy, pain in left side, urinary frequency and burning. Entered hospital March 20, 1921, B. P. 160/120. April 1, cystoscopy revealed severe cystitis (ureters and kidneys not examined). After delivery April 2, fever, unmistakable signs and symptoms of pyelitis, *B. coli* in urine. B. P. 140/95 on discharge, April 13.

CASE 24.—Born 1904. Dec. 2, 1929, 5 months pregnant, sore throat, cough and chills; Dec. 7, pain and tenderness in right flank, radiating downward, urinary frequency and burning, herpes, albumin, pus and blood in urine, B. P. 138/70, N.P.N. 35. Cystoscopy revealed bilateral pyelitis, *B. coli*. Cesarean section Jan. 10. Subsequent treatment in urologic clinic. Jan., 1933, urine negative, B. P. 120/74.

CASE 25.—Born 1902. 1918, pneumonia. Jan., 1924, scarlet fever, treated with serum, complicated by serum sickness and pyuria. Nov., 1924, curettage for incomplete abortion, B. P. 130/70, few leucocytes and red blood cells without albumin in urine. June, 1925, similar condition, slight albuminuria. Feb. 15, 1927, 7 months pregnant, B. P. 153/94, tenderness in both flanks, general edema, leucocytes and *Staph. aureus* in catheterized urine. Difficulty in voiding and pain on urination earlier in pregnancy. Delivered March 3, puerperium febrile. April 10, 1930, premature delivery after a week of vomiting, edema, albuminuria, B. P. 170/116, albumin, leucocytes and *B. coli* in urine. May 17, cystoscopy revealed cystitis, but no pyelitis. Sept. 29, renal lavage for *B. coli* pyelitis. May 21, 1931, pregnancy terminated after symptoms of pyelitis, because of edema, B. P. 200/130, chorio-

retinitis. May 3, no hydronephrosis by intravenous pyelography. Section of fallopian tubes June 13. Followed until Aug. 21, 1935, for dyspnea and palpitation without hypertension.

CASE 26.—Born 1890. Kidney trouble 1 month in first pregnancy, 1917. June 23, 1919, in last month of pregnancy, bilateral pyelitis of 2 months' duration diagnosed by cystoscopy. Delivered July 14, B. P. normal. Aug., 1927, early in pregnancy slight albuminuria without hypertension. Delivered Mar., 1928. Blood pressure, determined only at time of discharge, 110/70. April 23, B. P. 140/96, slight albuminuria. Still surviving Jan. 8, 1931.

CASE 27.—Born 1898. Cesarean section, 1928, for premature separation of placenta and albuminuria. 1930, cesarean at term for albuminuria and edema, B. P. 112/70, followed by ulcerative cystitis, treated until Feb. 10, 1934. No examinations of kidneys nor blood pressure.

CASE 28.—Born 1915. 1928, cellulitis of leg and urinary frequency. Sept., 1933, fibrosarcoma of right axilla removed, B. P. 132/88, minimal albumin and many leucocytes in urine. Oct. 15, 1935, near term, B. P. 156/110, albuminuria, edema of hands. Nov. 23, after delivery, right hydronephrosis and hydroureter by intravenous pyelography. Jan. 30, 1936, same by cystoscopy.

CASE 29.—Born 1918. Nov. 26, 1935, just before term in first pregnancy, after a month of slight edema, slight albuminuria, B. P. 146/95. Delivered Nov. 30. Dec. 7., mild right hydronephrosis by intravenous pyelography.

CASE 30.—Born 1897. 1917, second pregnancy terminated for hypertension, pain in back and sides, without albuminuria. Subsequent intermittent pain in flank. From August to December, 1920, headache, pain in back and hypertension. Sept., 1922, delivered at home, no albuminuria nor hypertension in August. Entered hospital Sept. 24, 1923, for chills, fever, urinary frequency and burning, with profuse pyuria, B. P. 170, phthalein excretion 45. Cystoscopy revealed cystitis and left pyelitis. Feb., 1925, after self-induced abortion at 5 months, albuminuria and pyuria. Nov., 1929, in sixth month B. P. 170/100. Dec., urinary frequency, dyspnea, edema of ankles, B. P. 200/100, N.P.N. 23, phthalein excretion 65. Urethral stricture, chronic cystitis and dilatation of both renal pelves found by cystoscopy. Stricture dilated. Delivered Mar. 10, 1930. Treated for hypertension and cardiac asthma until June, 1933.

CASE 31.—Born 1882. 1909, after stillbirth (third pregnancy) at term, pyelitis discovered. 1922, sharp pain in right flank. Oct., 1924, after similar pain in left flank cystoscopy revealed calculus at left ureteropelvic junction, dilatation of left renal pelvis, cocci and pus from both ureters. B. P. 178/100, heart enlarged. Calculus removed by pyelotomy. Increasing hypertension and associated symptoms until last visit, Apr., 1934.

CASE 32.—Born 1905. 1923, pregnancy terminated in fifth month for bilateral pyelitis. Chills, fever and pyuria in puerperium. Subsequently subcutaneous abscesses and blood culture containing nonhemolytic streptococci and *Staph. aureus.* Bilateral hydronephrosis found at cystoscopy. In subsequent pregnancies in 1928, 1933, 1934, and 1935, increasing signs of hypertension and heart failure with angina. Dec., 1935, B. P. 200/130, albumin and leucocytes in urine, N.P.N. and phthalein normal, moderate right hydronephrosis and hydroureter by intravenous pyelography.

CASE 33.—Born 1906. Kidney trouble 1908. Mar. 27, 1927, in fourth month of first pregnancy, pyuria, following tonsillitis, with chills and fever, treated elsewhere. Apr. 24, pyuria, B. P. 120/75, N.P.N. 32, phthalein excretion 60. May 27,

edema of feet. June 5, B. P. 148/88. July 31, disturbance of vision, B. P. 150/100. Aug. 5, during labor, convulsions. Puerperium febrile. Aug. 21, on discharge, pyuria persisted.

CASE 34.—Born 1905. Feb., 1927, early in first pregnancy pain in right flank, chills, fever, urinary frequency and burning. June 28, signs of acute pyelitis, fever, nonhemolytic streptococci in blood culture, no hypertension. July 13, perirectal abscess drained. Delivered elsewhere Oct. 3. 1928, miscarriage at 7 months. 1929, delivered elsewhere, fever and pyuria in puerperium. 1932, seen once in pregnancy at 3 months, condition unknown.

CASE 35.—Born 1893. 1923, 2 months after second delivery, urinary urgency, frequency and burning. 1927, increasing frontal headaches, 1928, pain in back, failing vision, followed later by palpitation, dyspnea, vomiting and frequent epistaxes. 1929, pus and *B. coli* in urine, advanced retinitis, B. P. 270/150, N.P.N. 33, phthalein excretion 40.

CASE 36.—Born 1900. 1928, in last month of pregnancy, albuminuria and pyuria. Ten days later slight retinal edema, B. P. 130/100, N.P.N. 26, phthalein excretion 60, *B. coli* in catheterized urine. Two weeks later, at term, edema of feet and ankles, puffiness of eyelids, retinitis. After delivery, fever, suprapubic pain and urinary frequency. Pyuria a month later. B. P. not elevated except as noted above.

CASE 37.—Born 1885. 1921, in fifth pregnancy terminated for hematuria, urinary frequency, headaches and palpitation. 1924, abortion at 2 months. Jan. 1, 1925, in fourth month, headache, epistaxis, urinary frequency, dyspnea, palpitation, B. P. 250/140. N.P.N. Feb. 11, 96, Feb. 20, 120; phthalein excretion 6, albumin, pus, blood and casts in urine. Left hospital against advice.

CASE 38.—Born 1896. 1929, early in first pregnancy, urinary frequency and burning with pyuria. Six weeks before term slight hypertension and edema. Recurrence of dysuria just before term. Febrile puerperium.

CASE 39.—Born 1905. Entered hospital in first labor Feb. 14, 1927, with edema of legs, B. P. 160/100, after period of edema, visual disturbances, urinary frequency and burning. Puerperium febrile, with pus in catheterized urine. May 9, backache, urinary frequency and burning and profuse pyuria, which had disappeared by June 25.

CASE 40.—Born 1895. 1925, kidney trouble in fifth month of pregnancy, but went to term. Renal condition and blood pressure aggravated during puerperium. Early in Jan., 1927, 4 months before term, increasing edema. Entered hospital Feb. 9, with general edema, retinitis and hypertension. After delivery Feb. 10, high fever, urinary frequency and burning, abdominal pain, bilateral costovertebral pain and pyuria.

CASE 41.—Born 1874. 1910, in second month of second pregnancy bilateral costovertebral pain and urinary burning. After delivery at term, convulsions, delirium, fever and urinary retention. Subsequently albuminuria and frequency. 1924, hypertension. 1926, headaches and edema of ankles. 1929, B. P. 184/100, heart enlarged, retinal arteriosclerosis. Steadily increasing hypertension with cardiac and renal failure until last seen in 1935 with B. P. 210/100, heart failure, fever, costovertebral tenderness, pus and *B. coli* in catheterized urine, N.P.N. 45 to 60.

CASE 42.—Born 1898. Mar. 24, 1926, albuminuria, B. P. 200. Delivered Apr. 5. Puerperium febrile with hypertension until Apr. 24, and frank pyuria throughout. June 11, B. P. 150/95, many leucocytes in urine. Mar., 1932, B. P. 140/88, urine clear.

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BLOOD AND PLASMA VOLUME CHANGES IN ECLAMPSIA*

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MARKED changes in many of the constituents of the blood occur during pregnancy. These changes in the blood and plasma volumes, hemoglobin and serum protein concentration are of such a magnitude that if the patient were not pregnant they would be considered abnormal and might be associated in many cases with characteristic symptoms and signs. Such alterations in blood volume in eclampsia and preeclampsia are intimately associated with the disease process.

During the past twelve years we have been studying various constituents in the blood and urine of toxemic patients. As soon as sufficient data were accumulated for one substance its determination was stopped, unless significant changes occurred. Thus during this period innumerable analyses were made, but the most marked changes, which were detected by frequent serial specimens of blood and which were of prognostic value, were in the hemoglobin, cell volume, and serum protein concentration in eclampsia and preeclampsia. These changes which may occur with extreme rapidity in many patients are due to alterations in blood and plasma volumes.

Table I illustrates the average and range for the hemoglobin, cell volume, and serum protein in patients with eclampsia. The day on which the convulsions and coma occurred is designated as "O," and the data are listed under days before

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TABLE I. BLOOD CHANGES IN ECLAMPSIA

PER CENT—AVERAGE	NO. OF DAYS BEFORE ECLAMPSIA			NO. OF DAYS AFTER ECLAMPSIA							
	2	1	0*	1	2	3	4	7	14	21	90
Hemoglobin†	87	96	108	95	93	97	89	84	84	93	103
Range	71-95	83-129	74-154	53-154	63-125	68-118	65-125	59-118	59-119	65-125	95-112
No. of patients	4	7	34	30	22	12	13	18	23	14	7
Cell volume	41	41	45	37	37	38	35	34	35	37	41
Range	31-49	32-48	35-57	27-51	27-50	28-46	24-52	23-50	25-45	27-42	36-46
No. of patients	5	13	42	33	25	14	13	26	26	14	10
Serum protein	5.7	6.0	6.7	5.3	5.4	5.1	5.4	6.0	6.7	6.8	7.2
Range	5.5-5.8	4.8-7.4	5.1-8.4	3.8-8.0	3.9-6.9	3.7-7.3	4.4-6.7	4.8-8.4	5.1-7.8	5.9-7.5	6.6-7.7
No. of patients	2	17	41	31	26	15	10	22	25	14	9

*0 = day of eclampsia.
†100 per cent hemoglobin = 13.8 gm. hemoglobin.

and after the occurrence of the acute disease. These studies were made on 97 patients with eclampsia, but a sufficient number of serial determinations were obtained on only 42. The convulsions and delivery occurred on the same day in 34 patients. Five patients had eclampsia two to nine days before, and three after delivery. The reduction in the concentration of hemoglobin, cell volume and serum protein without hemorrhage indicates an increase in blood and plasma volumes. An increase in the concentration indicates a shrinkage in the volume. These changes are not always parallel, but the direction of change is usually the same. Thus, for example, in one patient the hemoglobin dropped 37 per cent, the cell volume 34 per cent, and the serum protein only 25 per cent. The maximum average decrease in serum protein, amounting to 24 per cent, occurred on the third day and then there was a rapid return to the normal range by the fourteenth day. The maximum hemoglobin and cell volume reductions occurred on the seventh day and amounted to 22 and 25 per cent, respectively. By the third postpartum week the hemoglobin and cell volume concentrations were within the normal range. The increase in serum protein is slightly more rapid than in the hemoglobin and cell volume. Similarly, the increase in cell volume is more rapid than the hemoglobin. Occasionally, when a blood dilution occurs, the discrepancy between hemoglobin and cell volume is so great it gives the appearance that red blood cells were introduced, which contain a higher concentration of hemoglobin than that originally present.

Serial determinations of blood and plasma volumes were made, but, unfortunately, with the methods now available repeated determinations at short intervals do not give reliable results. Our average figures are listed in Table II. The difference in blood and plasma volumes between the normal pregnant and preeclamptic group is not significant. The number of eclamptic patients is too small to be of value. It is obvious, however, that both groups, especially the latter one, show a definite decrease in blood volume. Rowntree and Brown designate this condition as a polycythemic hypovolemia (a decrease in both blood and plasma, but a greater

TABLE II. VOLUME PER KILOGRAM OF BODY WEIGHT

	NO. OF PATIENTS	BLOOD—C.C.		PLASMA—C.C.	
		AVERAGE	RANGE	AVERAGE	RANGE
Nonpregnant women*	25	85.7	77- 94	51.7	45-58
Normal pregnancy	55	80.9	55-115	49.8	35-65
Vascular-renal disease	29	83.2	69-105	50.9	45-65
Preeclampsia	14	77.5	65- 95	47.0	35-55
Eclampsia	6	71.4	67- 78	39.4	33-46

*Rowntree, L., and Brown, G.: The Volume of Blood and Plasma, Philadelphia, 1929, W. B. Saunders Co.

decrease in the latter than the former, resulting in a proportionally greater cell volume). Three of the eclamptic patients with the small blood volumes died.

Fig. 1 illustrates graphically the changes in hemoglobin, cell volume, and serum protein which occurred before, during, and after eclampsia in three patients. The first patient, E. R., who had a severe preeclampsia with a subnormal blood and plasma volume, showed an increase in the hemoglobin, cell volume, and serum protein of 12, 21 and 28 per cent while under treatment, or an average reduction in the blood volume of 20 per cent. The blood pressure increased, the urine volume decreased, and headache and visual symptoms appeared simultaneously. Labor was induced, but within a few hours convulsions and coma developed. Coma was still present forty-eight hours after delivery and the patient regained consciousness only after an injection of gum acacia solution which initiated a blood dilution, a diuresis and clinical improvement. If the blood and plasma volumes at

the sixth postpartum week were normal for this patient, whose weight was 14 kg. less, then the volumes determined before the convulsion were markedly below normal.

The second case illustrates the reduction in hemoglobin, cell volume and serum protein, or an increase of blood volume amounting to 18 per cent, coincidental with the cure of the convulsions and coma seven days before delivery. Our treatment consisted of intramuscular injections of 25 per cent magnesium sulphate and intravenous injections of 1000 c.c. of 20 per cent glucose solution at six- to eight-hour intervals.
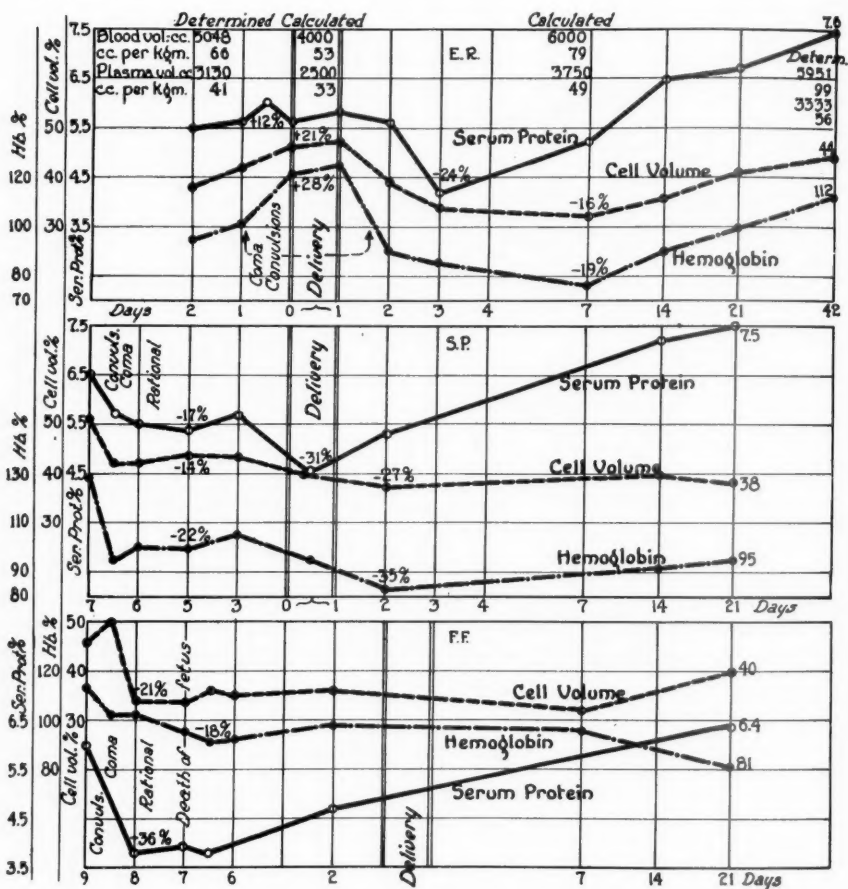
Fig. 1.—Graphs illustrating the plasma and blood volume changes which occurred in three patients with eclampsia.

The third case, F. F., also illustrates the blood dilution which occurred simultaneously with the cessation of convulsions, return of consciousness and diuresis. The fetus died forty-eight hours after admission of the patient. The calculated average increase in blood and plasma volumes amounted to 23 per cent.

Table III lists the average changes in blood and plasma volumes as determined by changes in hemoglobin, cell volume and serum protein. The figure for the initial determinations was used as the divisor and the difference between it and the figure for the greatest increase or decrease was the dividend. The quotient was multiplied by 100. The three quotients were added together and an average figure

was obtained. This figure was assumed to represent the alteration in blood volume. If the hemoglobin, cell volume and serum protein increased, the blood and plasma volumes decreased, and vice versa.

Column (a) represents those patients in whom one or more blood specimens were obtained two hours to seven days before the onset of convulsions. Twelve patients showed a reduction in blood volume of from 7 to 46 per cent, as convulsions and coma occurred. These patients showed comparable increases in volume after delivery, as indicated in Column (b).

TABLE III. BLOOD VOLUME CHANGES IN ECLAMPSIA

RANGE OF CHANGE PER CENT	PREECLAMPSIA → ECLAMPSIA		ANTEPARTUM OR POSTPARTUM ECLAMPSIA	AFTER INTRAPARTUM ECLAMPSIA AND DELIVERY	
	ANTEPARTUM	POSTPARTUM			
	DECREASE	INCREASE	INCREASE	DECREASE	INCREASE
	(a)	(b)	(c)	(d)	(e)
1- 9	5			2	2
10-19	2	3	4	1	11
20-29	2	3	4		9
30-39	2	5			3
40-49	1				
Total	12	11	8	3	25

Column (c) contains data from eight patients, five of whom had antepartum, and three postpartum, eclampsia. The convulsions in the former group occurred 2, 6, 7, 9, and 9 days, respectively, before delivery. There was no blood loss in this group. The changes in volume in the postpartum group resemble those of the antepartum group so closely that we do not believe they were due to the blood loss of 200 to 300 c.c. occurring at the time of delivery.

Columns (d) and (e) contain data from patients in whom the onset of the eclampsia preceded the delivery, but both occurred on the same day. Three patients showed a further decrease in blood volume while under treatment. Two of them died. After delivery the increase ranged from 7 to 39 per cent.

Blood studies were available in three patients who died. They showed average decreases in the blood volume as follows: 11, 17, and 14 per cent. The amount of blood in three of these was 69, 78, and 69 c.c., and the plasma was 39, 39, and 32 c.c. per kilogram of body weight.

Fig. 2 illustrates the changes in cell volume and serum protein during normal and toxemic pregnancy. Dieckmann and Wegner have demonstrated, by serial determinations of blood and plasma volumes, hemoglobin, cell volume, and serum protein concentration on the same patients, that the increase in plasma volume is 25 per cent and the blood volume is 23 per cent at term. Therefore, although there is a decrease in the concentration of hemoglobin, cell volume, and serum protein, the total amount of each is increased. No adequate explanation for these changes has been advanced. In a previous article, using similar methods, the author demonstrated that the changes in the concentration of hemoglobin, cell volume, and serum protein in the vascular-renal group (chronic nephritis in pregnancy) were parallel to those of normal pregnancy. However, preeclamptic patients showed changes similar to those of eclampsia. The fact that the graphs for these latter two conditions are almost identical indicates the close relationship of preeclampsia to eclampsia. The cerebral, visual, and gastrointestinal symptoms, and the oliguria of preeclampsia and eclampsia are directly associated with the blood concentration. The amelioration or cure of these symptoms likewise occurs with a blood dilution. The height of the blood pressure, degree of albuminuria, or amount of edema does not always parallel the changes in blood volume.

DISCUSSION

The increase in hemoglobin, cell volume, and serum protein is caused by the passage of water as a dialysate containing electrolytes, glucose, and the nonprotein nitrogen constituents into the tissues. Serum protein escapes into the tissue spaces and some of the erythrocytes may be stored in the spleen and others stagnate in the capillaries of the muscles if the blood concentration is prolonged. The reverse process occurs as the blood dilutes, and water, electrolytes, etc., pass into the blood stream. A blood dilution occurs after hemorrhage. If the reduction in the hemoglobin, cell volume, and serum protein occurred only after delivery the most probable explanation would be that it is the result of the blood dilution taking place after the blood loss incidental to delivery. The fact that a blood dilution was observed five
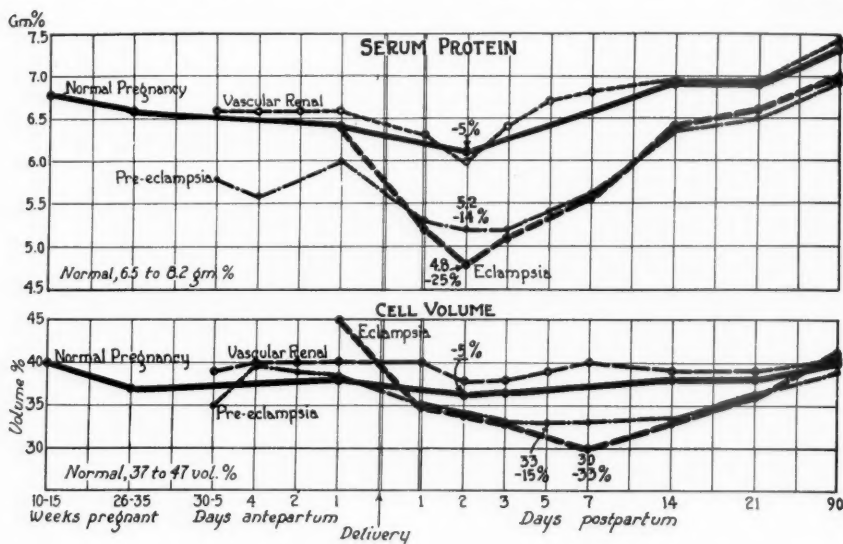
Fig. 2.—Graphs illustrating the average changes as determined by serial examinations of the blood. The figures for eclampsia are based on 21 eclamptic patients, and differ slightly from those in Table I, which are based on 42 patients.

times before delivery indicates that hemorrhage is not a factor. Furthermore, the blood was more concentrated in fifteen cases, thus indicating the need for a subsequent dilution or return to the normal. The hemoglobin, cell volume, and serum protein concentration may drop below the normal because of an overcompensation by the vascular system, but the normal volume is established within a few days. There is no constant relationship between the degree of blood dilution and the amount of edema.

The observations of Rowntree and Brown on patients, and Dieckmann and Wegner on themselves and patients, demonstrate that the blood and plasma volumes, hemoglobin, cell volume, and serum protein concentration tend to be constant for the individual under normal

conditions. Disease or markedly abnormal practices, such as the excessive ingestion of water, deliberate dehydration, or excessive exercise, will cause changes, but as soon as conditions are normal, the hemoglobin, cell volume and serum protein, and in all probability the blood and plasma volumes, return to their usual amount.

The blood dilution which occurs after delivery in toxemic patients was discussed by Schwarz and Dieckmann in 1929, with a review of the literature. They demonstrated that clinical improvement in eclampsia was associated with a blood dilution. Failure of the blood to dilute with their usual treatment indicated that the eclampsia was of the severe type and that delivery offered the only hope for the mother.

Skajaa determined the cell volume of a large number of normal and toxemic patients and reported his results in 1929. He stated that an average blood concentration of 15 per cent, or condensation, as he termed it, occurred during labor in toxemic patients. Those patients showing a greater concentration also evidenced symptoms of greater severity in the toxemias. Blood dilution was accompanied by abatement of the symptoms. He stated that the greatest condensation was found in impending eclampsia, amounting to 23 per cent before labor and to 30 per cent during labor. The average blood dilution amounted to 25 per cent during convalescence. One patient showed a 78 per cent decrease in cell volume.

The reports by Skajaa and by Schwarz and Dieckmann were published independently of each other in 1929. The results and conclusions are identical.

Table IV contains data from a group of diseases which are associated with a blood concentration. It has been only within the past decade that the clinician has become cognizant of the importance of a concentration of the blood. The data in the table indicate that the amount of fluid usually given parenterally, necessary to restore the blood and plasma volumes to normal, ranges from 93 to 843 c.c. per hour. It is obvious that the administration of small amounts of fluid is of little value. The treatment of these various conditions necessitates the regulation of the water balance by the determination of hemoglobin, cell volume, or serum protein, or by the hourly measurement of the urine. The latter plus one of the blood constituents is the ideal method.

It has been demonstrated repeatedly that shock is associated with a hemoconcentration, but the results of Underhill and coworkers in the treatment of severe burns with large amounts of fluid first indicated the clinical importance of reduction in blood volume. They demonstrated conclusively that the hyperpyrexia, tachycardia, delirium, oliguria, and high mortality in extensive burns was associated with a tremendous increase in hemoglobin concentration, indicative of a blood concentration, but that if sufficient fluids were given to lower the hemoglobin to normal, these symptoms and signs disappeared or were abated in degree and recovery usually occurred.

TABLE IV. VARIOUS DISEASES CHARACTERIZED BY BLOOD CONCENTRATION

	PARENTERAL AND ORAL FLUID—C.C. IN GIVEN TIME	TIME FOR CHANGE HR.	HB. PER CENT	CELL VOLUME PER CENT	SERUM PROTEIN GM. PER CENT	HB., CELL VOLUME, SERUM PROTEIN, CHANGE PER CENT	RATE PER 24 HR. AND RATE PER HOUR—C.C.
Hyperemesis gravidarum	10,500 + 550 c.c. blood	42	100 69	45 30	6.2 4.1	31 decrease 33 decrease 34 decrease	3,810 158
Preeclampsia → eclampsia; labor	500 + oral	18	83 105	32 55	4.7 5.6	27 increase 72 increase 19 increase	
Eclampsia	3,400 intrav. 7,800 oral	36	111 59	42 27	6.4 4.4	47 decrease 36 decrease 31 decrease	7,464 311
Intestinal obstruction	8,060	36	125 100	48 39	6.6 5.1	20 decrease 23 decrease 23 decrease	2,240 93
Diabetic coma Ralli, E., and Waterhouse, A.: Am. J. M. Sc. 187: 607, 1934.	5,000 4,270 oral	11	111 97	50 39		13 decrease 22 decrease	20,330 843
Severe burns Underhill, F., et al.: Arch. Int. Med. 32: 31, 1923.	16,450	67	230 126			46 decrease	2,450 102
Bilateral adrenalectomy in dog Swingle, W., Vars, H., and Parkins, W.: Am. J. Physiol. 109: 488, 1934.	With extract No extract	120	83 129	38 54	6.3 7.7	51 increase 42 increase 22 increase	

Peters and coworkers, Ralli and Waterhouse, and other investigators have described the concentration of the blood in diabetic coma, as indicated by the high hemoglobin, cell volume or serum protein concentration, compared with the figures for these substances when the diabetes is under control. They noted that an oliguria or anuria was present with the concentrated blood. If urine could be obtained, it contained remarkably low concentrations of nitrogen and sodium chloride. The concentration of these substances in the urine increased rapidly as the condition of the patients improved and the blood became diluted. We have made similar observations in eclamptic patients. They have pointed out that there is no parallelism between hemoglobin and serum protein changes, but that the direction of change is the same. They also noted that a failure of the blood to dilute or a reappearance of the blood concentration indicated a change for the worse in the clinical condition. They stated, furthermore, that a delay in the restoration of serum volume and blood concentration is a more accurate criterion for determining the prognosis than either blood sugar or carbon dioxide determination.

Himwich has demonstrated that the lack of water in depancreatized dogs causes a blood concentration, as evidenced by increased specific gravity, osmotic pressure and hemoglobin concentration. The administration of water cures the various symptoms and signs. The result of these changes, as depicted by him and to which we have made certain additions, is as follows:

DECREASED BLOOD VOLUME

Decrease in blood supply to skin $\rightarrow$ Hyperpyrexia
Decrease in blood supply to muscle $\rightarrow$ Lactic acid
Decrease in blood supply to kidney $\rightarrow$ Nitrogen and acid retention
Increase in blood viscosity $\rightarrow$ Additional work for heart $\rightarrow$ Tachycardia $\rightarrow$

Myocarditis

Changes in EKG similar to those of insufficient oxygen supply to heart.

Marked reductions in blood and plasma volumes are associated with cholera, the anhydremia of babies, and severe protracted vomiting from any cause. The administration of adequate amounts of fluid usually causes marked improvement in the disease. Bilateral adrenalectomy in the dog results in a blood concentration which can be cured by the parenteral administration of extract of the adrenal cortex.

Friedlander, Silbert and Laskey have stated in several reports (1) that the blood volume is decreased after thyroidectomy or oophorectomy in the experimental animal; (2) oophorectomy in a young woman is distinguished by a decrease in blood volume; (3) that the blood volume is decreased in thrombo-angiitis obliterans; and (4) that the administration of thyroid extract will cause an increase in it. Thompson noted a 23 per cent increase in the plasma volume of patients with myxedema

following the administration of thyroid extract. There appears to be some relation between blood and plasma volumes and diminished function of the adrenal and thyroid glands and the ovaries. While it is tempting to theorize on the regulation of blood volume by one of these glands, it is obvious that many more observations must be made before any conclusions can be drawn.

CONCLUSIONS

1. A concentration of the blood, which may be relative (below the average for the period of pregnancy) or absolute (less than the normal for the nonpregnant patient), occurs in eclampsia.

2. This concentration can be demonstrated by blood and plasma volume determinations, but it is best demonstrated by serial determinations of hemoglobin, cell volume, or serum protein concentration. The change in concentration of these substances is not always parallel, but the direction of change is usually the same.

3. A concentration of the blood and plasma is not the cause of the eclampsia, but it is intimately associated with the convulsions, coma, oliguria, and the various cerebral, visual, and gastrointestinal symptoms. A blood dilution is associated with clinical improvement as determined by a diuresis, cessation of the convulsion, return to consciousness, decrease in temperature, pulse, etc.

4. Death occurred in three patients in whom a permanent blood dilution could not be maintained.

5. Since the exact cause of eclampsia is unknown and a concentration of the blood occurs which may be so marked as to be incompatible with life, treatment which will dilute the blood should be instituted. Innumerable methods of treatment have been used. If the case is mild almost any type of treatment, provided it carries no mortality of its own, is efficacious. If the case is severe, treatment which comprises control of the convulsion, dilution of the blood, and relatively early delivery must be instituted.

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BLOOD LIPIDS IN PREECLAMPSIA*

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I T HAS been previously shown in this JOURNAL[1] that the convulsive and preconvulsive stages of eclampsia are characterized by a significant increase in the ratio of phospholipid to total cholesterol values of blood plasma. At that time it was intimated that a further study of this relationship was being made in cases diagnosed as preeclampsia in an effort to determine if this ill-defined condition could be subdivided on the basis of the plasma P/TC ratio. The present report is concerned with blood lipid findings in 49 cases of preeclampsia. Previous literature on this subject has been covered in the former communication.[1] Professor H. Kürten of Munich has kindly informed the author that he had already suggested that lipid ratios were of significance in the toxemias of pregnancy and eclampsia in a paper published in 1924.[2]

The present series of cases were of severe or relatively severe preeclampsia. The patients exhibited hypertension, albuminuria and edema all of considerable extent. In addition many complained of headaches, visual disturbances, and oliguria. Renal function tests (phenolphthalein excretion, urea clearance, polyuria, etc.) occasionally indicated some impairment of renal activity but the results were not consistent. Likewise the usual blood chemistry findings were of a variable nature (urea, uric acid, creatinine, sugar, carbon dioxide, etc.). All patients were at or near the termination of pregnancy, and there was no history or other evidence of chronic nephritis in the group herein reported. Mild toxemias with slight hypertension or albuminuria have not been included in this series, although in incidence they comprised about an equal number to the more severe cases and most of them, for the lack of data to the contrary, were diagnosed as preeclampsia.

An oxalated specimen of blood was obtained in the morning usually under fasting conditions. All patients were hospitalized at the time blood was taken, and under these conditions breakfast does not appreciably affect plasma lipid values of normal persons,[4] but there may be a slight difference in the values of the red blood cells.[5] Potassium oxalate as an anticoagulant tends to dilute plasma resulting in about 10 per cent lower values for the lipids[6] but oxalated blood was used in the previous studies of normal pregnancy and eclampsia with which it was desired to

compare the present results. Extracts of plasma and of the red blood cells were prepared and each was analyzed by the author's modification of Bloor's oxidative microtechnic.[7, 8]

When the cases were considered collectively by means and standard deviations, there appeared to be no significant variations from the corresponding values for normal pregnancy.[3] Since the significant variation found in eclampsia was an increase in the plasma P/TC ratio, a frequency distribution curve of this value in preeclampsia was prepared. This is shown in Fig. 1. It is obvious that there are two peaks in the distribution and that it is possible to construct two frequency curves. This indicated that there were two types of cases in the preeclamptic
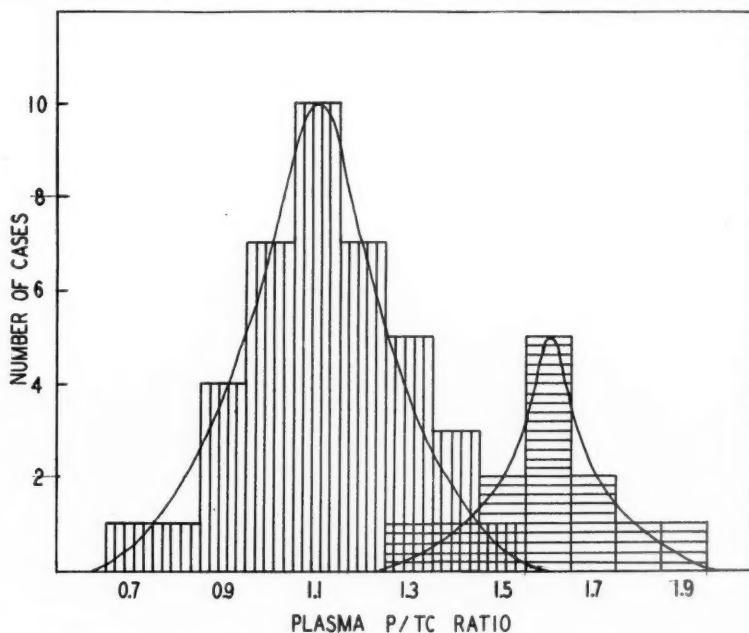
Fig. 1.—The frequency distribution of values for the plasma P/TC ratio in 49 cases of preeclampsia.

group, one having a relatively normal plasma P/TC ratio and another smaller group in which the ratio was elevated as in eclampsia.

An arbitrary ratio value of 1.5 was taken as the dividing line and the cases tabulated into two groups according to whether their ratio was above or below 1.5. It is recognized that a few cases of the lower ratio group might have values above 1.5 in a large series and that a few cases of the higher ratio group might be below 1.5. To be on the safe side when a question of therapy is involved, the author advises the use of 1.4 as the lower limit for potential eclamptics since values in the 1.4 class have been found in eclampsia.[1] The value of 1.5 was selected now since it was desired to compare lipid values for plasma and the red blood

cells in the two groups and 1.5 appeared to be the nearest delineation statistically. The value of the ratio depends, of course, upon the methods used for phospholipid and total cholesterol, but it would appear possible to employ methods other than those used by the author, providing the normal range and the range in the two groups of preeclampsia be first established.

A comparison of plasma lipid values in the normal and high ratio groups of preeclampsia is given in Table I. The complete tabulation of all values would require the presentation of some one thousand figures,

TABLE I. AN ANALYSIS OF THE LIPID VALUES FOUND IN BLOOD PLASMA IN PRE-ECLAMPSIA; THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF PLASMA

VALUE	TOTAL LIPID	COMPOSITION OF TOTAL LIPID						LIPID RATIOS		
		NEU-TRAL FAT	TOTAL FATTY ACIDS	CHOLESTEROL			PHOS-PHO-LIPID	P/TC	P/FC	P/EC
				TOTAL	ESTER	FREE				
Normal Ratio Group (38 Cases)										
Minimum Total lipid	655	126	365	211	148	63	219	1.04	3.48	1.48
Maximum Total lipid	1380	553	910	322	211	111	364	1.13	3.28	1.72
Mean values	953	342	613	235	162	73	268	1.14	3.67	1.65
Standard deviation	208	122	171	49	46	16	55	0.17	0.58	0.12
Standard deviation in per cent of mean	22%	36%	28%	21%	28%	22%	21%	15%	16%	7%
High Ratio Group (11 Cases)										
Minimum Total lipid	840	97	482	213	161	52	422	1.98	8.10	2.62
Maximum Total lipid	1350	382	742	321	205	116	510	1.59	4.40	2.49
Mean values	990	352	651	206	127	79	347	1.68	4.40	2.73
Standard deviation	181	183	128	58	51	24	80	0.26	0.79	0.74
Standard deviation in per cent of mean	18%	52%	20%	28%	40%	30%	23%	16%	18%	27%

and hence a statistical method has been employed. The formula used for calculating the standard deviation has been previously given in this JOURNAL.[1]

It may be seen from Table I that there were no marked differences in the plasma lipid values between the two types of preeclampsia. The high ratio group tended to have higher values for all lipids except ester cholesterol which was low and consequently produced a low total cholesterol. Along with this tendency to a low ester cholesterol, plasma phospholipid was somewhat higher in the high ratio group. Comparing mean values, ester cholesterol was 28 per cent lower and phospholipid 37 per cent higher in the high than in the normal ratio group of preeclampsia. In no case was the range of values in one group beyond the

range in the other as calculated from the means and standard deviations. Practically all the plasma lipid values in both groups of preeclampsia were higher than those previously found in normal pregnancy,[3] but the differences were in no case sufficiently great to extend the expected range beyond that of normal gravidas. It may be concluded that this group of the toxemias of pregnancy tends to exhibit a slightly greater lipemia than normal pregnancy, but this is of academic interest only since cases even of eclampsia may show relatively low plasma lipid values.[1] From the practical point of view, one cannot distinguish preeclampsia from normal pregnancy by comparing plasma lipid values in any one given case.

On the other hand there is evident a significant difference in the phospholipid to cholesterol ratios. In the normal ratio group of preeclampsia, the mean value of the plasma P/TC ratio was 1.14 with a standard deviation of 0.17. This mean plus the standard deviation in this group ($= 1.31$) was thus lower than the mean minus the standard deviation of the high ratio group ($1.68 - 0.26 = 1.42$). Statistically, approximately 75 per cent of cases of the high ratio group may be expected to have plasma P/TC ratios above 75 per cent cases in the low or normal ratio group. Practically, this would appear to be a ready means of distinguishing between these two types of preeclampsia. On reviewing the case histories in relation to the subdivision of preeclampsia by means of the plasma P/TC ratios, it was found impossible to designate any further symptomatic difference between the types. In general the high ratio group showed more severe symptoms, but this was far from an absolute rule. In view of the similarity in findings between the high ratio group of preeclampsia and eclampsia itself,[1] it is offered that the two conditions represent one and the same disease, in the one case without and in the other case with convulsions. On the other hand, the majority of cases now included under the diagnosis of preeclampsia do not appear to be literally preeclamptic at all. Of the present series, 38 cases out of 49 were of a normal ratio (? noneclamptic) type or 78 per cent of the whole group. Since many milder cases diagnosed as preeclampsia were not included in this study, it is likely that the incidence of high ratio cases (? truly preeclamptic) would be not more than 10 per cent of the whole group.

Plasma cholesterol is composed of two fractions, a free or unbound type and cholesterol linked with fatty acids to form cholesterol esters. This latter fraction is usually designated ester cholesterol. In the plasma of normal persons, cholesterol esters constitute by weight the lipid of greatest bulk present. The question arose as to whether only the ratio of phospholipid to total cholesterol (P/TC) was the significant difference or if there were also significance differences in the ratio of phospholipid to free (P/FC) and to ester cholesterol (P/EC). Hence these latter

two ratios were also calculated and a statistical analysis of the results included in Table I. It may be seen that the P/FC ratio was higher in the high ratio group but that the ranges overlapped. However, a real difference existed in the P/EC ratios: the mean plus the standard deviation of the normal ratio group $(1.65 + 0.12 = 1.77)$ was lower than the mean minus the standard deviation of the high ratio group $(2.73 - 0.74 = 1.99)$. In fact the differences were of the same order of magnitude as those of the P/TC ratio. There would thus appear to be some disturbance in the normal balance between plasma phospholipid and plasma cholesterol esters in this group of preeclampsia, and it may be noted at this point that these two lipids constitute the bulk of all lipids normally present in human blood plasma. The, let us say, truly preeclamptic group may thus be distinguished from the remaining cases of preeclampsia by the plasma P/EC ratio as well as the plasma P/TC ratio. As a matter of fact it is easier to determine total cholesterol than ester cholesterol by the author's technic and by most other methods of lipid analysis. So that there is little to be gained and more work involved in determining the P/EC ratio rather than the P/TC ratio.

The significance of the phospholipid to cholesterol ratios is further evidenced by a comparison of their relative variation with that of the actual lipids. This has been shown in Table I under "standard deviation in percent of mean." It may be seen that in practically all cases there was less relative variation in the lipid ratios than in the actual lipid values. This would indicate that whereas the lipids themselves may vary considerably in value, there is a tendency toward the maintenance of a relatively constant ratio between them.

The lipid composition of the red blood cells in the two groups of preeclampsia has been given in Table II. In general, it may be said that the red cells of the normal ratio group contained slightly more of almost all lipids than was found in the red cells of normal gravidas,[3] while those of the high ratio group contained slightly less than healthy pregnant women. This may be seen only in the means and is not apparent from individual cases, nor is the range of one group beyond the range of the other. From the first few cases studied, it was calculated that there was a significant increase in red cell neutral fat in the nonconvulsive toxemias,[9] but further studies indicated, as herein pointed out, that this difference was not as great as was at first thought.

The relative variations of the red cell lipids are well illustrated in Table II. Neutral fat and cholesterol esters were found to be extremely variable and usually present in small quantities only. These red cell extracts were prepared in the conventional manner by heating for a short time the alcohol-ether extract of the hemolyzed cells. This procedure introduced colored decomposition products of hemoglobin, and from work now in progress, it is apparent that this colored matter tends

to give false high values for all lipids and especially neutral fat. However the same method of extraction was used in the eclamptic cases and a comparable one in normal pregnancy with both of which the present values have been compared. The lipids least variable in amount in the red cells were phospholipid and cholesterol, and these together constitute the bulk of red cell lipids.

TABLE II. AN ANALYSIS OF LIPID VALUES FOUND IN THE RED BLOOD CELLS IN PRE-ECLAMPSIA; THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF RED CELLS

VALUE	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					
		NEU-TRAL FAT	TOTAL FATTY ACIDS	CHOLESTEROL			PHOS-PHO-LIPID
				TOTAL	ESTER	FREE	
Normal Ratio Group							
Minimum							
Total lipid	418	169	289	60	0	60	191
Maximum							
Total lipid	1067	377	732	128	0	128	562
Mean values	626	103	362	135	20	115	374
Standard deviation	177	142	142	35	31	34	95
Standard deviation in per cent of mean	28%	138%	39%	26%	155%	30%	26%
High Ratio Group							
Minimum							
Total lipid	236	0	112	69	0	69	167
Maximum							
Total lipid	805	311	540	127	0	127	367
Mean values	519	77	299	118	29	89	310
Standard deviation	181	118	139	37	37	26	74
Standard deviation in per cent of mean	35%	153%	47%	31%	128%	29%	24%

DISCUSSION

It has been shown that plotting the frequency distribution of plasma P/TC ratios in preeclampsia reveals the presence of two types of cases, one with a normal range of ratio values and a smaller group with elevated ratios. The findings in the latter group were comparable to those previously found in eclampsia. Hence, it is postulated that the high ratio group of preeclampsia represents cases of eclampsia without convulsions, while the normal ratio group may be an entirely separate condition. It cannot be gainsaid on present information that cases with a normal ratio may not go on to a high ratio if left untreated, and this point is being further investigated. From the small amount of data now available, it does not appear that a normal ratio commonly, if at all, becomes an increased one.

A statistical comparison of plasma and red cell lipids revealed that no lipid value possessed a range, determined from the mean plus and minus the standard deviation, significantly different in one group from the range in the other. The high ratio group of preeclampsia tended to have a slightly greater plasma lipid content and slightly lower red cell lipid

content on the average. The high ratio in this group was due chiefly to relatively higher values for phospholipid and lower values for ester cholesterol.

These several observations indicate some disturbance in lipid metabolism. It has been known for many years that lipid metabolism is altered in pregnancy, and the present work has shown that there occurs a further abnormal change in eclampsia and in a group which may be separated from what we now diagnose as preeclampsia. The nature of this disturbance in lipid metabolism has been, and still is, enveloped in obscurity; its cause, its importance, its effect, even its nature are largely unknown. In the past few years the author has been interested in these problems, but in spite of a good deal of work barely more than the surface has been scratched. It has been shown that the lipemia of pregnancy in women is analogous chemically to lipemias in other conditions and is characterized by an orderly increase in plasma lipid values with no change in the lipids of the red blood cells.[3] Following parturition, the lipemia gradually subsides, but if normal lactation be prevented, a further lipemia supervenes which may be taken to indicate that the drying up of the breasts, though frequently resorted to, is in reality pathologic.[10] At the end of pregnancy, the leucocyte count is usually elevated, but the lipid content of the white cells is not significantly changed: after labor there is an increase in the phospholipid and free cholesterol of the blood leucocytes (indicative of increased activity) and an increase in neutral fat which latter probably represents a scavenger action on the part of the white cells in removing débris fat from the involuting uterus.[11]

Evidence has been presented that the human placenta is "permeable" to lipids and that a good deal of fatty substances, especially phospholipids, is absorbed by the human fetus from the umbilical circulation, suggesting that one result of the lipemia in the mother may possibly be the nourishment of the infant in utero.[12] The latter part of pregnancy in rabbits[13] and guinea pigs[14] was found associated with evidence of increased lipid metabolism in the placenta, suggesting that the placental tissues may be actively engaged in the transfer of lipids from the mother to the offspring. In the rabbit it was found that a marked increase in the lipid content of the fetus does not occur until the latter third or so of gestation,[13] at which time the lipid metabolism of the placenta also increases.

It does not appear that the lipemia of pregnancy in women is of toxic origin, since an even greater lipemia may occur in the lower animals, for example guinea pigs.[15] There is a certain amount of direct evidence that the changes in endocrine balance during pregnancy may have something to do with the changes in the concentration of blood lipids. By comparing blood lipid values in pregnant and pseudopregnant rabbits, it was possible to show that in early gestation certain

changes may be due to the direct or indirect effects of the products of conception and other changes to the direct or indirect effects of the presence of the corpus luteum.[16]   In the rabbit, in which a lipopenia or decrease in blood lipid values occurs during pregnancy (for the use of the term lipopenia see Boyd[17]), there is a marked rise and fall in the lipid composition of the ovary.[18]   On the other hand a lipemia is found during pregnancy in guinea pigs as in women[15] and practically no change occurs in the lipid content of guinea pig ovaries throughout gestation.[19]   The author has also found in unpublished experiments the phospholipid and free cholesterol content of the human ovary to be quite low at the end of pregnancy in one or two cases studied.   This evidence points to the endocrine system as a factor in the disturbed lipid metabolism of pregnancy but is far from sufficient to establish the exact relationship.

SUMMARY

The lipid composition of blood plasma and of the red blood cells was determined by oxidative micromethods in 49 cases of preeclampsia.

On the basis of the plasma P/TC ratio it was possible to show that these cases could be divided into two groups, one with a normal P/TC ratio and one in which the ratio was elevated as in eclampsia.

Cases with a high plasma P/TC ratio tended to have slightly higher plasma lipid values and slightly lower red cell lipid values than cases of a normal ratio.

The increase in the plasma P/TC ratio was due chiefly to relatively high plasma phospholipid and relatively low plasma ester cholesterol values.

It is offered that cases of preeclampsia with a high ratio are in reality eclampsia without convulsions, while the remaining normal ratio cases are not literally preeclamptic at all.

The significance of changes in lipid metabolism during gestation has been discussed.

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THERAPEUTIC ABORTION BY MEANS OF X-RAY*

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TEN years ago the Gynecological Service and the Radiotherapy Department of Mt. Sinai Hospital attempted a preliminary series of therapeutic abortions by means of x-ray. This was stimulated by the favorable report of Ganzoni and Widmer in 1925. The results obtained were sufficiently satisfactory to warrant a continuation of the method. We wish to report the results of our experience of ten years with the records of 200 fully studied consecutive cases.

The necessity for therapeutic abortion has been diminished somewhat in recent years. In part, this is due to a more general knowledge of contraception and, in part, to the more definite attention given this vital prophylactic service by physicians. There still occur too many pregnancies that should, perhaps, have been avoided. We attribute to our systematic campaign in bringing this to the attention of our hospital staff, the fact that we have a relatively small number of therapeutic abortions, of which those by x-ray outnumber other methods. It should be noted, as well, that many of these patients were not seen in our wards or out-patient departments prior to their pregnancy.

In the search for a surgically ideal method which would eliminate the mortality and morbidity of therapeutically indicated abortion, roentgen rays were thought of long ago. Experiments in the interruption of pregnancy were made before 1907 (M. Fraenkel), but the early reports must be discounted because of the unreliability and uncertainty of the dosage. It is only since the era of accurate dosage measurement and improved x-ray apparatus, that we can estimate the results.

Routinely, when the question of interruption arises, a consultation is held between the representatives of the gynecologic, the radiotherapy department and the department in charge of the indicating condition. At this consultation, both the question of intervention and the method are decided. The patient, is, of course, informed of the possibility of a permanent amenorrhea, and written consent is obtained. Our indications have been medical only, not economic or eugenic. Multiparity plays a rôle only when the existence of a sufficiently large family makes it unfair to ask the patient to assume an extraordinary risk for the sake of progeny.

After radiation has been decided upon, the patient is prepared, an enema is given, and the pelvis is rayed by means of the technic which will be described later on. When the treatment is completed, the woman is instructed to return at weekly intervals and/or at the first sign of bleeding or cramps. These usually occur about three to four weeks after treatment, and the patient is then admitted to the hospital. Ordinarily, she spontaneously aborts, expelling a dead fetus, most often enclosed in an intact sac. Usually there is only slight bleeding compared with that seen in an ordinary miscarriage. The convalescence is quite uniformly uneventful and the patient is in a condition to be discharged from the hospital in a few days, though she is usually kept somewhat longer.

Instruction is given to avoid intercourse in the interval between treatment and abortion. One woman who failed to do this and contracted gonorrhea, ran a postoperative febrile course as a result of pelvic infection in sharp contrast to the uniformly uneventful convalescence of the others.

Upon discharge, patients are referred to our follow-up, also to the contraceptive clinic for advice to be followed, even though they are amenorrheic. Occasionally, due either to lack of cooperation or (far less likely) to failure of contraception, a second pregnancy results. The treatment can then be repeated. We have seven successful repetitions of the treatment, all of these patients remaining amenorrheic to date.

In some cases, the sac ruptures and the fetus and placenta are expelled attached to each other. Much less often the placenta is retained for a brief time. The subsequent involution is quite uniformly satisfactory. Retention of fragments does not follow as it does so frequently when a live fetus is surgically removed.

In the event of premonitory bleeding, when examination shows a gaping cervix, we have frequently administered small doses of pituitrin which expedite the completion of the delivery. It is probable that slight staining, especially with a closed cervix, should be treated with a dose of "patience." If, however, examination reveals an ovum stuck in a *dilated* cervical canal, a simple twist of a forceps suffices to terminate the whole process. This requires no anesthesia and should not be classified as an operation.

We believe that the abortion is caused by the death of the fetus as a direct result of the radiation, rather than through any effect on the ovaries or the placenta. Since young growing cells have a greater sensitivity to x-ray than older ones, one can destroy the fetus without any considerable damage to the uterine musculature and the parametrial tissues. The entire lymphatic apparatus is the most sensitive of the tissues. On the other hand, Momigliano, in his work on irradiated rabbits, seems to have shown definite changes in the placenta, shutting off fetal nutrition. We have not been able to find unequivocal changes in the placenta in our cases.

These cases are, in reality, excellent examples of missed abortions. We know that the fetus dies sometime before the expulsion of the uterine contents (usually fourteen days after treatment), and cannot be differentiated from the morphologic picture of missed abortion. The fetus is flattened, loses its typical translucency, the vessels cannot be seen through the skin, which is macerated, the amniotic fluid is dark brown and turbid as in missed abortion, expulsion is preceded by a stage of spotting and the discharge of thin fluid, followed by cramps.

According to Von Graefe, the retention in the uterus of the dead products may be related to a decreased irritability of the uterus. Taussig agrees that the gradual death of the fetus permits an adaptation so that it does not act as a foreign body so promptly. What does eventually initiate the uterine contractions is not definitely known, though doubtless the answer will be forthcoming as a result of our rapidly increasing knowledge of the interplay of the internal secretions.

METHOD

The technic used throughout this series of cases was uniform. Sixty per cent of a skin erythema dose (600 r. measured in air is considered an erythema dose) was given to the center of the uterus. Calculation of the amount that had to be given to the skin to obtain this dose was determined by making outlines of the pelvis and estimating the quantity necessary to obtain the desired dose in the uterus according to the methods of Holfelder and Weatherwax. In the average case with an anteroposterior pelvic diameter of 20 cm., two opposing fields each receiving 600 r. in air will suffice if the apparatus will deliver 35 per cent S.E.D. at 10 cm. depth. When the anteroposterior diameter is larger than 20 cm., compression cones or strapping of a pendulous abdomen will aid in reducing the distance to the uterus. When adequate reduction of the distance is not possible, additional portals of entry (three to six) may be required.

The apparatus should be calibrated by a competent physicist and if possible a constant reading dosimeter between the tube and the patient will aid in giving the correct dosage. The physical factors are 180-200 K.V., 50 cm. F.S.D., filter 0.5 mm. copper 1 mm. aluminum, size of portals average 15 × 20 cm. (suprapubic and sacral including the adnexa). The treatment should be given on two or three successive days.

A mild cathartic is given on the evening before treatment and the bladder is always emptied immediately before treatment is administered. The outline of the uterus is mapped out on the anterior abdominal wall with a colored pencil and the central beam is directed through the middle of the fundus.

When there is a discrepancy between the length of amenorrhea and the size of the uterus, we advise a radiograph of the pelvis to determine if possible the size of the fetus. The presence of fibroids is not a contraindication to treatment.

It is most important to keep certain facts in mind in the case management after radiation. Since the time interval varies so, we must be very patient, and if convinced that the embryo is not growing, be content to wait. No harm can result. Febrile and toxic symptoms do not develop.

The checks on viability are the absence of growth (controlled by weekly examinations), the Aschheim-Zondek or Friedman test, which may, however, remain positive for some weeks, and the test for female sex hormone which becomes negative even when the Aschheim-Zondek test remains positive.

If continued growth, etc., convince us that the fetus is still alive after four weeks, radiation may be repeated, provided that the size of the uterus at that time is not larger than that of a four months' pregnancy. There are several instances in this series in which this procedure was carried out successfully.

The pregnancy must never be permitted to continue to term, following x-ray treatment, because of the definite possibility of the birth of an abnormal child.

Wintz believes that 50 per cent of children who have received such large antenatal radiation will be pathologic. Goldstein and Wechsler have demonstrated definite eye changes in the form of typical rosettes of infiltrating cells in the retina, etc., in our material.

The possible effect on subsequent pregnancies is undecided and seems far more doubtful. We know of five such pregnancies and, so far, the children have seemed perfectly normal. E. Maurer reports fourteen children of irradiated mothers, none of whom were abnormal. He concludes from the literature that one cannot speak for or against the safety of conceiving after radiation. Of 229 such children, 25 per cent showed some pathologic findings, but critical sifting reduces this to a very small number in which one could possibly attribute the defect to the radiation. In 1931, the German Society for Heredity issued a warning of possible injury to the germ cell which might become manifested only after a number of generations.

We agree that it should be made clear to candidates for this treatment that they should not plan to have more children, and the treatment should be restricted to patients who are willing to cooperate fully in this respect, and in whom the indications are permanent and absolute.

CASE REPORTS

We are reporting 200 fully studied cases. Of these patients, all but 8 aborted dead fetuses. That would give a 96 per cent success. However, of these there were 12, or 6 per cent, in whom the sac or the

placenta was removed from the cervix or uterus without anesthesia.   If we exclude these cases as partial failures from the standpoint of a perfect method, we have been 90 per cent successful.

The ages of the patients varied from sixteen to forty-eight, the average being thirty-two.   The parity varied from no children to 14, with an average number of 3 children to a woman.   Many had had previous surgical abortions, often with stormy convalescences.   Twenty-two, or 11 per cent, aborted at home (with

Fig. 1.—Illustrating the fetus and placenta expelled in an intact sac, following roentgen treatment.
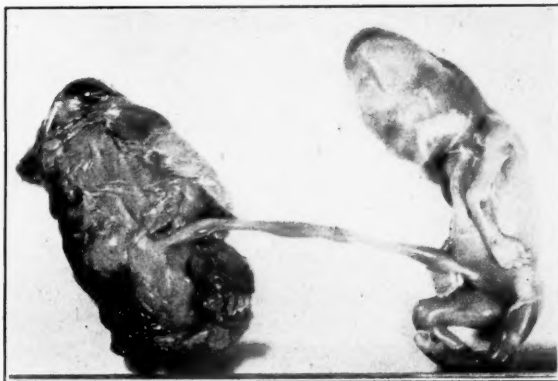
Fig. 2.—Illustrating fetus and placenta expelled after rupture of the sac.   The fetuses are in varying stages of flattening and maceration.

so few symptoms that they did not think it necessary to come to the hospital). The average hospital stay of the others was nine days.   This would be misleading if we did not remember that we are dealing with a debilitated group, the longer hospital stay necessitated by the general medical condition which was the indication for intervention.

The interval between treatment and abortion varied from three days to one hundred and fifty, the majority, 60 per cent, occurring between the nineteenth

and thirty-fifth days. The average was thirty-three days. The occasional very rapid or very long delayed abortions are quite exceptional. We are sure that many of the reported failures, including some of our own earlier cases, were mistakes in judgment and instances of needless interference as evidenced by the findings. The amount of bleeding was usually slight. In 12, it was moderate, in 5 profuse, but always easily controlled. The period of amenorrhea afterward was very variable. In general, it can be stated that almost all of the patients below the age of twenty-five will have a return of menstruation though the amenorrhea may vary from one to forty-eight months. In the patients from twenty-five to thirty, one-half have remained amenorrheic so far. Of those who were thirty to thirty-five, slightly more than half. In the age group thirty-five to forty, about two-thirds, and those over forty, all became amenorrheic. In no case can we promise that menstruation will surely return. The majority of the patients had some menopausal symptoms. These are not easy to evaluate. According to the records of our follow-up, they were, in most instances, mild. Wintz calls attention to the milder menopause in women rayed during the period of amenorrhea, and feels that this is related to the fact that the endocrine system is, in a sense, adapted to amenorrhea and adjusts itself more easily. Certainly the complaints of our patients on this score were in no way a major problem in this series.
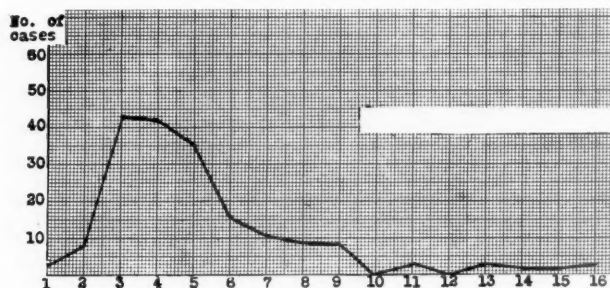
Chart 1.—Graph showing interval in weeks between application of roentgen therapy and the subsequent abortion in 200 successive cases.

The patients have been followed, in most instances, for many years. Unfortunately, with a shifting population, this has not always been possible. Ideally, it is most important, as we noted return of menstruation with subsequent pregnancy as long as fifty-four months after treatment. (In this interesting case, a vesicovaginal fistula had been cured in the meantime, and the patient so extraordinarily improved in health that it was possible for her to go through a normal pregnancy. She delivered an apparently healthy child.) No patients died from the treatment. Several women in this series have died of the associated medical lesion or some intercurrent condition, some time afterward.

TABLE I

Number of cases—200	
Failures	8 – 4%
Requiring removal with forceps—without anesthesia	12 – 6%
Completely successful	90%
Clinically successful	96%
Died—none	
Morbidity	
Fever	2 – 1%
Sharp bleeding	4 – 2%
Repetition of pregnancy	8 – 4%
Repetition of treatment	7 – 3.5%

The abortions were performed for the following indications: A. *Very frequent:* Chronic cardiac valvular disease, 74 cases; pulmonary tuberculosis, 27 cases; and Graves' disease, 19 cases.   These three lesions represent two-thirds of all the cases.

B. *Not infrequent:* Postoperative (especially following recent operations for large central hernias or tuberculous kidney), 16 cases; nephritis, 12 cases; and malignant psychoneurosis, 9 cases.

C. *Occasional indications:* Mental deficiency, 4 cases; malignant hypertension, 4 cases; severe diabetes, 4 cases; surgical tuberculosis, 4 cases; and asthma, 4 cases.

D. *Among rare indications are included:* Arthritis with ankylosis, 2 cases; congenital cardiac disease, 2 cases; pelvic cellulitis, 2 cases; Hodgkin's disease, 1 case; Banti's disease, 1 case; retinitis proliferans, 1 case; ulcerative colitis, 1 case; spinal cord tumor, 1 case; glaucoma, 1 case; and extreme malnutrition, 1 case.

We have been particularly interested in the psychologic effect of this whole procedure.   Some authors have emphasized the mental strain involved in asking these women to wait over an extended period of time for the completion of the abortion. Some have been concerned with the question of the loss of libido.   Our own observations have led us to believe that in this type of patient suffering from some severe organic disease, the mental attitude after x-ray abortion is not bad, if we have prepared the patient by preliminary instruction and reassurance.   A very few have complained of diminution of libido and loss of orgasm.   This is just as likely to be psychogenic in origin and would not be unexpected in any series of 200 women followed for a period of time.   In the cases of malignant psychoneurosis, we are dealing with women in whom we cannot evaluate loss of libido or orgasm so simply. A most careful estimate of the personality of the patients in this group and the possible traumatic effect is imperative for obvious reasons.

If one could shorten the period between death of the fetus and expulsion, it might be an improvement in the method.   Wintz feels that the inclusion of the ovaries in the irradiated field is vital, to eliminate the possibility of preserving a glandular function of the ovary which might inhibit expulsion.

The failures may be classified into two groups: (1) complete failures and (2) clinical failures.   A complete failure refers to the cases in which the fetus was not dead and continued to grow.   Clinical failure refers to those cases in which the fetus was killed but where there was retention of a portion of the products of conception, usually a fragment of placenta in the gaping cervix.

Of the 8 failures enumerated in Table II, Case 1 should be classified as a clinical failure.   Although the patient in Case 4 felt life before treatment was instituted, the roentgen method was tried because of the severity of the patient's cardiac condition. A dead fetus was expelled shortly after the introduction of a Voorhees' bag, and it is quite likely that the fetus would have been expelled spontaneously had we waited.   The same is true in Cases 3 and 8.   Review of the treatment in Case 5 showed definite undertreatment.   No definite reason for failure could be found in the remaining 3 cases other than possible faulty technic.

The advantages of the method include the absence of morbidity in patients in whom an anesthesia is dangerous, especially the cardiac, tuberculous, and nephritic patients; the absence of any mortality, in respect to which this method is incomparably superior; the absence of infection, since there is no introduction of a foreign body into the uterus; the minimal bleeding due to the mummification of the fetus and closure of the blood sinuses; the avoidance of retention of products of conception and the period of amenorrhea which seems to be of some value in cases of pulmonary tuberculosis.   It might be interesting to compare 200 hospital cases of therapeutic abortion reported by P. Kühnel.   These were done by skilled operators.   There were 2 operative deaths, severe hemorrhage in 16, infections in 36, tears of the cervix in 18, and "accidents" in 22, including 2 perforations of the uterus.

The disadvantages should be carefully considered: The method may fail. Then we are confronted with the necessity of performing a surgical abortion at a somewhat later time. Then there is the possibility that a patient will insist on a subsequent pregnancy and delivery, and although we have not as yet seen any deleterious effects on later children, the subject has not been studied for a sufficiently long time for any categoric statement. Then there is the question of the menopause symptoms which may persist for years, and the loss of libido complained of in a few cases.

The disadvantages must be weighed in every individual case against the disadvantages of either a curettage or a hysterotomy. It should be superfluous for me to warn against the wholesale application of such a method. In early pregnancy in

TABLE II. FAILURES IN 200 CASES OF ROENTGEN THERAPEUTIC ABORTION

	NAME	AGE	ADMISSION	GRAVID—WK.	TREATMENT	RESULT
1	G. W. (Tbc.)	32	4/30/26	8	5/ 1/26 5/ 2/26	5/23/26 Placenta removed from cervix
2	R. R. (s. c. tumor)	31	2/18/36	12-14	2/19/26 2/20/26	Bag introduced 4/17/26
3	E. S. (C. C. V. D.)	36	3/18/27	12	3/22/27 3/23/27	4/19/27 Hysterotomy
4	L. K. (C. C. V. D.)	37	10/ 2/29	8 Felt life	10/ 2/29 10/ 3/20	11/7/19
5	L. R. (C. C. V. D.)	25	6/22/29	8	6/24/29 6/25/29 (Under-treated)	11/11/29 Bag introduced
6	L. G. (Tbc.)	30	7/11/31	8	7/ 8/31 7/ 9/31	Spotted cramps 8/12/31 Hysterectomy 11/19/31
7	A. H. (C. C. V. D.)	25	3/ 5/30	12	9/ 9/30 9/10/30	1/3/31 Bougie introduced
8	M. R. (asthma)	25	12/25/32	8	12/28/32 12/20/32	2/27/33 Hysterotomy

a debilitated patient with an acute exacerbation of a chronic disease, especially tuberculosis or severe cardiac disease, when subsequent pregnancies are absolutely interdicted, it seems ideal. Now and then it offers a way out when one's hands are otherwise tied. Although the total percentage of patients in whom this method can or should be used may be small, if we consider that 60,000 to 80,000 therapeutic abortions are performed annually with a heavy toll in mortality and morbidity (Taussig), there would seem to be an actually large number of women who could be saved by this method.

SUMMARY

We are reporting ten years of experience with therapeutic abortions by x-ray.

We have had 200 ward patients with a clinical success in 96 per cent and an ideal success in 90 per cent.

The method is recommended for pregnancies of not more than fourteen weeks' duration, in women who are suffering from a serious lesion

which would make surgical interruption very dangerous and who should not again become pregnant. This is particularly valid for women over thirty-five years of age.

The method has no mortality and remarkably low morbidity, but it does require the closest cooperation between clinician, radiotherapist, and gynecologist, as well as scrupulous observation, control, and follow-up of the patient.

If the treatment should fail, under no circumstances should the pregnancy be permitted to continue.

Irrespective of amenorrhea, patients should receive contraceptive instruction after the abortion.

The clinical picture is that of a missed abortion with a latent interval averaging about four and one-half weeks.

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DISCUSSION

DR. SEYMOUR WIMPFHEIMER.—Usually the menopausal symptoms after this x-ray method do not seem to affect the patient's condition adversely, and I have followed the blood pressures in several cases over a number of years and found very little change. I have carried out this method in eleven cases at Montefiore Hospital. Six of the patients were seriously ill with pulmonary tuberculosis, four were suffering from cardiac disease, two of whom were in cardiac failure. We were successful in all our cases. The method and the results in the main coincided with those given by Mayer and Harris.

DR. IRA I. KAPLAN.—We have tried altogether 8 cases at Bellevue Hospital in the course of the past ten years. We have not used the x-ray method of producing abortion more frequently, because we have not been successful. The description of the technic as given by Harris shows me that our technic was entirely different. Yet we have been successful in sterilizing a great many patients, and it is hard for me to realize just now why our abortion results were so unsuccessful.

The first case that we tried was a woman thirty-six years of age who two years previously had had a surgical abortion and x-ray sterilization because of recurrent carcinoma of the breast. For a year she had remained amenorrheic but in October, 1926, reported to us that she was pregnant. We gave her an intensive course of

x-ray therapy and waited seventeen days, but no abortion occurred. She was then referred to Dr. Holden who did a hysterotomy and found twins. The specimens were sent to Streeter of the Department of Embryology of the Carnegie Institute, who reported as follows: ''The tissues in both the chorion and the embryo are greatly macerated, indicating that death had occurred a long time before abortion. We assume the period of development to be 10½ weeks.''

The second case had a marked pulmonary tuberculosis, a gravida iv, para i and at the time we were asked to see her was pregnant two or three months. She received x-ray therapy, and we waited six weeks. No abortion occurring, hysterotomy was done in April, 1927, and a macerated fetus was removed. In January, 1928, after almost nine months of complete amenorrhea, she reported to us with definite signs of pregnancy. The question arose as to whether we should abort her on account of the previous x-ray sterilization, but she was permitted to go to term and was delivered of a perfectly normal baby. This child is now 8 years old and perfectly normal. The mother has no evidence of active tuberculosis and has menstruated normally since her last delivery.

Our third case was that of a colored woman, twenty-one years of age, para i, whom we saw in March, 1927. She had active pulmonary tuberculosis and her previous pregnancy had ended only four months previously. She was first treated by pneumothorax to control the tuberculosis and was then given x-ray therapy when about two and a half months pregnant. We waited five weeks and she suddenly aborted. That was the first successful result we had had.

The fourth patient, seen in December, 1927, was a little hunchback with marked anemia, who had been pregnant ten times previously and had had three miscarriages. She had seven living children. We gave her x-ray when the pregnancy was at three months and waited seven weeks, but nothing occurred and hysterotomy was then performed. I will read to you later Dr. Streeter's report of this case and the next one.

The fifth patient, seen in January, 1928, was a white woman, thirty-seven years old, gravida ix, with very severe tuberculosis. She was given x-ray therapy when two months pregnant, but after seven weeks, nothing having happened, hysterotomy was performed.

The fetuses from the two previous cases were sent to Dr. Streeter. He wrote that the baby of the first case appeared to be normal, nineteen to twenty weeks of age. The other, Streeter said, was ten weeks old. He believed that these fetuses must have been living up to the time of abortion. ''After the pregnancy has started and has developed past one month,'' Dr. Streeter says, ''it is too late to damage the fetus without damaging at the same time the mother.'' His subsequent report on these fetuses, after sectioning, was that there was no damage to the tissues.

The sixth case was one of carcinoma of the cervix. The patient came to us about two months pregnant. She was given x-ray therapy, but no abortion occurred. She continued to term and had a normal child, delivered through the carcinomatous cervix. The child was found to be perfectly normal at the time of delivery in May, 1929, at another hospital. The mother was well for a time after radium treatment of the carcinoma of the cervix.

In July, 1933, the seventh case, a woman with severe tuberculosis and a cardiac condition, gravida ii, two months pregnant, was treated by x-ray therapy. She spontaneously aborted after seven weeks. One month after this she was operated upon in the Bellevue Hospital for acute peritonitis which it was proved followed the perforation of a tuberculous tube.

On Jan. 5, 1934, we accepted the eighth patient, whose diagnosis was pulmonary tuberculosis with pneumothorax and gynecologic tuberculosis. She was a gravida i,

para 0, now two months pregnant, although the Aschheim-Zondek test was reported negative. Six weeks after treatment, no abortion having taken place, she was operated upon and a living four-and-one-half-month-old fetus removed.

Thus of 8 patients treated, only two have been successful. We conclude therefore that radiation given during pregnancy is not always followed by abortion. Radiation so given is usually fatal to the very young fetus, but normal children may be born. Nevertheless if the woman does not abort, we think that surgical abortion should be performed.

DR. WILLIAM E. STUDDIFORD.—I would like to say a word or two in defense of operative therapeutic abortion.

There are not many conditions in which one cannot perform an operative abortion if there is a skillful anesthetist at hand. There are no failures, and if therapeutic abortion is properly done—and that means the complete removal of the ovum—there should be no hemorrhage. The incidence of infection is not great.

One of the city medical examiners told me the other day that he had never had a case of therapeutic abortion come to his attention at autopsy as a medical examiner's case.

DR. HENRY T. BURNS.—There are very few cases where there is a contraindication to operation and, as far as anesthesia is concerned, I have done 8 or 9 therapeutic abortions under a local, using novocaine, which works very nicely and with very little discomfort. We use one-half of 1 per cent novocaine solution along the base of the broad ligament and also under the bladder fold and wait about five minutes for the novocaine to take effect. The best results follow in women who have never borne children, because there is no scar tissue about the cervix to interfere with infiltration of the novocaine.

DR. NELSON B. SACKETT.—I would like to report the case of one patient admitted to Woman's Hospital when three and one-half months pregnant with carcinoma of the cervix involving the entire portio vaginalis. We gave her the usual dose of radium to the cervix, assuming that abortion would follow soon afterward. During the next three weeks, with the Aschheim-Zondek test persistently positive, the patient had a few vague pains, stained a few times but did not abort. We decided then to employ roentgen therapy, and she was given 800 r. units through each of four portals in eight days. Despite all that treatment she still failed to abort, although the Aschheim-Zondek test now became negative. The carcinoma had shown virtually no regression under this treatment, and eventually the patient came to Wertheim hysterectomy after which she died.

I merely mention this experience as an example of the type of case where a great deal of irradiation by x-rays and radium fails to produce abortion, although we assume that the fetus was killed by the radiation. The hysterectomy specimen revealed a shriveled, complete ovum and an undilated cervix infiltrated with carcinoma.

DR. C. FREDERICK JELLINGHAUS.—I feel the indications mentioned by the speaker were rather broad. For example, some patients with Graves' disease can have their thyroid operated upon, the pregnancy being allowed to go to term. He stated an internist, a gynecologist, and a radiologist decided whether the abortion was indicated or not. I should suggest adding an obstetrician to aid in making the decision.

The speaker stated there is always a risk of amenorrhea after the x-ray treatment and that in patients between twenty-five and thirty years of age amenorrhea

followed in 50 per cent. I am mid-Victorian and believe in the old adage: "A woman's best friend is her menstruation," and for this reason I think in most cases the x-ray method of bringing on an abortion is wrong.

DR. WILLIAM H. CARY.—One point that Dr. Mayer's paper did not make perfectly clear to me concerns the most favorable time in pregnancy for the application of the irradiation. Assuming that a very early diagnosis is made, should some time necessarily pass before the irradiation? In all the cases reported the fetus and placenta were both definitely developed.

DR. FRANK R. SMITH.—I would like to ask the speakers just what they consider a sterilizing dose of x-ray. I have delivered patients who received 1,800 mg. hours of radium in the uterus and had become pregnant afterward. I have had one patient in fact who received 2,500 mc. hr. of radium in the cervix while pregnant, and went to term.

DR. MAX D. MAYER (closing).—In answer to Dr. Jellinghaus. I am willing to disclose the records of every one of these 200 cases to any member of the Society and believe that they will agree that not one of these patients should have been permitted to continue their pregnancy. I feel that an average of 20 therapeutic abortions annually for a hospital the size of Mount Sinai with a 750-bed capacity is not excessive.

Answering Dr. Cary's question about the time, I would say that there was always an interval between the diagnosis of pregnancy and the decision, which time was, in most cases, occupied in studying the patient.

DR. WILLIAM HARRIS (closing).—There were a number of cases in this group where the only alternatives were hysterotomy or roentgen therapy for the termination of the pregnancy. This was especially true in four cases with ankylosing arthritis of both hips where pelvic examination could be performed only with the patient absolutely flat, and where no operative procedure could be done by the vaginal route.

We have had surgical mortalities from therapeutic abortion. One patient refused the menopause that would follow roentgen abortion, and curettage resulted in an anesthetic death. We have done a few abortions with local anesthesia around the cervix, but the majority of these cases presented by Dr. Mayer were crippled patients who certainly would have had some morbidity if not mortality had surgical intervention been used.

I am afraid that Dr. Kaplan was using the phrase sterilizing effect of radiation rather loosely. Forty per cent of an erythema dose is enough to stop any patient from menstruating for a while; it will stop a patient over forty years of age completely. We should not use the word sterilizing, but instead should say the production of an amenorrhea by irradiation because you are not always sure of sterilization unless massive doses are given. We have had patients who became pregnant during the amenorrheic phase, several patients under thirty-five years of age, and one between thirty-five and forty.

One can definitely sterilize a patient even in the strict sense of the term. You render a patient amenorrheic so that she will not conceive again if you give three series of 40 per cent of an erythema dose each, or three times 240 r. to the ovaries within one year. Now the reason that a patient may menstruate after the insertion of a radium tube in a cancer of the cervix is because the radium tube is placed in the cervix and from this position one gets very little irradiation from the end of a radium tube into the fundus. When one gives 1,800 mg. hours in the endometrial cavity, the

main effect is on the endometrium with very little effect on the ovary. The amenorrhea produced is due chiefly to the secondary effect on the ovaries from destruction of the endometrium.

You do not get very much radiation effect at the end of a radium tube; you get it mainly at right angles to the tube. That explains why you can get menstruation, or why pregnancy will continue after a maximum dose for carcinoma of the cervix is given with a tube which does not extend beyond the internal os.

CALCIUM AND PHOSPHATASE STUDIES IN CANCER OF THE FEMALE SEX WITH A CONSIDERATION OF BASAL METABOLIC RATE AND URINE pH

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IN PREVIOUS reports we have shown that the apparent calcium deficiency shown by blood and, more particularly, blister fluid of patients with malignant disease is related to decreased protein content of the fluids. Because of recent interesting and contradicting reports of the relation of phosphatase to malignancy.[3-7] we have continued our work with the addition of phosphatase values. On the same series of cases we have determinations of basal metabolic rate and urinary pH. The cancer group contains cases of gynecologic malignancy while our control series is taken from the same ward, but has no known malignancy.

METHODS

Collection of samples and determination of the various chemical constituents have been described in our previous paper.[2] Phosphatase values were determined by the King and Armstrong[8] method. Preliminary experience with this method gave us difficulty with turbidity which was avoided by omitting the Li_2SO_4 from the phenol reagent. Private communication with Armstrong has confirmed the need of this modification in some cases, with no effect on the accuracy of the method. All samples were analyzed as soon as taken. This is especially important, since Bodansky[9] has noted increase in phosphatase on standing. This change may be due to change in pH of the blood serum, according to Woodard and coworkers.[6] Control determinations using thymol blue indicator for spot testing have shown that our substrate-serum mixture has a pH of 8.7 before and after digestion. The substrate after standing two months becomes slightly more alkaline and slightly higher values are obtained. This increase is of the order of 5 per cent with a substrate two months old, and since the substrate we used was always less than one month old and none of the serums would have abnormal pH, our results are not affected by pH change. The phosphatase values are for pH 8.7 ± 0.1.

For basal metabolic rate determinations we are indebted to Mrs. Mildred Woodward here. The Benedict-Roth apparatus was used and corrections were applied for height, weight, and body temperature. Each case was run after sixteen hours' fasting, and each was a hospital patient brought to the laboratory while in bed. The average of two determinations is taken for the final reading.

Urinary pH determinations were run on a fasting morning specimen obtained by catheter and compared in a LaMotte indicator block within fifteen minutes after collection.

RESULTS

Table I gives the results obtained for 26 cases with no demonstrable malignancy. Twenty-four of these were diagnosed by surgical biopsy as fibroids, cervical polyps, hyperplastic endometrium, pelvic inflammation, and tuberculosis of the uterus. One was a case of cystocele and rectocele, and the other a case of vesicovaginal and recto-vaginal fistulas following radium treatment for cancer of the cervix six years ago, who is now cancer free as proved by biopsy and laparotomy.

Table II gives the results on 50 cases of malignancy, each of which was diagnosed by biopsy.

Table III gives a summary of the minimum, maximum, and average values of each of the determinations.

DISCUSSION

Results for calcium, inorganic phosphorus and protein correspond with our former series of cases.[2] It is interesting to note that average protein and calcium values in both blood and blister fluid run slightly higher than the former series, and inorganic phosphorus values run slightly lower. This we attribute to seasonal difference. Most of the present series were run in the summer months when vitamin intake, sunlight, and balanced diet had more influence than on our former series of cases during the winter and spring.

This second set of cases affirms our former conclusion that there is no change in calcium and phosphorus metabolism in malignancy that is not related to changes in protein content of the body fluids as influenced by malnutrition, cachexia, or chronic loss of albumin.

The additional set of values for calcium ion concentrations, reported here, confirm our former finding that malignant disease does not affect the calcium ion concentration of blood serum (calculated according to McLean and Hastings[10]), and that in malignancy there is very likely no change in parathyroid function.

With the exception of Case 69 (Table I) and Cases 14, 26, 27, 33, 31, 36, 42 (Table II), the phosphatase values in both series of cases are within normal limits. The last three cases, 31, 36, and 42, are only slightly above the limit set by King and Armstrong and according to the work by Yaguda[11] may be within the normal for the method. Case 69 of our nonmalignant group with a phosphatase value of 21.6 units seems to show that occasionally the normal value may exceed 12 units, as we have no explanations for the raised value here. We have sought particularly evidence for Paget's disease[11, 12] or liver damage[11, 13] but found none. Cases 14 and 33 are patients with probable liver metastases, as this was considered a possibility by physical examination, and the appearance of the liver of Case 33 at operation was suggestive of cirrhosis or metastatic carcinoma with no visible tumors. Gutman et al.[12] have reported phosphatase increase in metastases to liver. For Cases 26 and 27 we have no explanation for the high phosphatase values. The patient in Case 26 is in good health one year after radium treatment. The patient in Case 27 died at home seven months after treatment. It is possible that bone or liver metastases may

TABLE I. RESULTS ON NONMALIGNANT CASES

CASE	DIAGNOSIS*	AGE	BLOOD					BLISTER FLUID					URINE pH	BMR
			Ca	P	Pr	pH	Ca++	Ca	P	Pr	pH	Ca++		
8	Cervical polyp	72	10.33	3.71	6.87	6.5	4.6	9.29	3.85	6.24	6.6	4.4	-	-
10	Fistulae	50	10.63	4.25	7.32	3.9	4.6	8.95	4.31	6.15	3.8	4.3	7.6	-
15	Hyper. endometrium	42	10.70	4.41	7.56	4.2	4.5	8.82	4.41	5.88	8.6	4.3	5.4	+16.0
17	Hyper. endomet., polyp	50	10.32	3.90	7.80	6.3	4.3	7.90	3.88	6.36	4.9	3.6	4.8	-12.7
18	Hyper. endomet., P. I. D.	22	10.44	4.27	7.68	4.2	4.4	9.20	4.40	6.36	3.6	4.3	5.8	-5.9
21	Hyper. endometrium	40	9.20	2.72	4.23	4.1	5.2	8.00	2.81	3.54	4.2	4.9	5.1	+6.0
22	Hyper. endometrium	39	9.80	2.43	6.30	4.7	4.6	8.73	2.69	4.90	6.5	4.6	5.4	+12.5
23	Hyper. endometrium	36	10.80	2.38	7.98	4.8	4.4	9.20	2.63	6.24	5.4	4.3	5.2	+9.0
24	Hyper. endometrium	37	10.00	2.78	7.62	9.8	4.2	8.98	3.03	6.24	10.8	4.2	5.3	+4.3
32	Retained secundines	50	9.80	2.64	5.88	5.9	4.8	8.43	2.78	4.98	3.9	4.5	5.2	-1.4
34	Fibroids	36	10.01	3.37	7.23	9.0	4.4	8.80	2.50	6.36	8.0	4.1	5.5	-5.6
35	Ov. cyst, atroph. endomet.	30	10.38	3.16	7.20	4.5	4.5	8.55	3.44	6.06	3.8	4.1	7.1	-6.8
37	Cervical polyp	46	10.75	3.97	6.99	6.8	4.8	9.30	4.41	6.06	4.8	4.5	5.4	-4.0
38	Chronic cervicitis	46	9.60	2.50	6.24	9.0	4.5	7.95	2.53	5.19	9.3	4.1	6.4	+1.0
40	Hyper. endomet., fibroid	49	10.00	3.44	6.03	12.5	4.8	8.65	3.66	4.74	9.6	4.7	6.1	-4.5
43	Hyper. endometrium	48	10.80	2.81	6.54	8.3	5.0	9.12	2.84	5.22	6.3	4.7	7.2	-3.6
48	Fibroids, arthritis	50	10.22	4.28	7.11	9.7	4.5	8.70	4.34	5.64	6.8	4.3	4.6	+9.5
53	Cervical polyps	50	10.30	3.06	7.44	7.2	4.4	8.55	3.80	5.64	5.6	4.2	6.4	+0.4
55	Cervical polyps	36	10.21	3.20	6.66	5.3	4.7	8.92	3.41	5.82	5.6	4.3	5.0	-4.3
61	Metrorrh., hypothyroid	16	10.05	3.18	6.96	8.8	4.5	8.75	3.38	5.40	8.6	4.5	5.3	-14.3
62	Inflammation vagina	62	10.38	3.96	7.62	7.5	4.4	9.00	4.10	6.18	5.4	4.3	6.2	+0.5
64	Hyper. endometrium	40	10.73	3.55	6.90	10.8	4.8	9.30	3.75	6.15	9.9	4.4	5.0	+30.0
68	Hyper. endometrium	41	10.16	3.25	6.30	10.1	4.8	8.28	2.31	4.80	9.6	4.4	7.1	-
69	T. B. of uterus	45	11.03	3.52	7.32	21.6	4.8	8.69	3.44	6.45	20.2	4.0	7.4	+10.8
74	Hypertension, fibroids	49	10.20	3.73	8.10	6.0	4.2	8.68	3.69	6.15	4.5	4.2	7.2	+12.0
75	Cysto- and rectocele	54	10.50	4.04	7.98	5.6	4.3	8.98	4.41	6.00	3.9	4.3	7.2	-1.3
	Average	43.7	10.27	3.40	6.99	7.52	4.57	8.77	3.58	5.77	6.94	4.33	5.73	+2.5

Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca++) are expressed in mg. per 100 c.c., age in years, serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong units, urine pH in units, and basal metabolic rate (BMR) in per cent deviation from normal.

*Abbreviations used for diagnosis:

Atroph., atrophic; Endomet., endometrium; Hyper., hyperplastic; Metrorrh., metrorrhagia; Ov., ovarian; P. I. D., pelvic inflammatory disease; T.B., tuberculosis.

TABLE II. RESULTS ON CASES OF PROVED MALIGNANCY

CASE	DIAGNOSIS*	AGE	BLOOD					BLISTER FLUID					URINE pH	BMR
			Ca	P	Pr	pH	Ca++	Ca	P	Pr	pH	Ca++		
1	Met. Ca. of Ing. glands	31	11.03	4.22	7.92	5.1	4.6	9.06	3.81	6.12	3.9	4.3	—	—
2	Ca. of urethra	61	10.33	4.09	5.10	3.8	5.4	—	—	—	3.8	—	—	—
3	Ad.-Ca. of ovary	56	9.70	2.00	6.66	8.6	4.5	9.10	1.81	5.64	6.3	4.5	—	—
4	Ca. of cervix	63	9.92	3.10	7.02	5.9	4.4	—	—	—	—	—	—	—
5	Ca. of cervix	62	9.20	2.78	6.69	8.0	4.1	7.83	2.81	5.28	11.7	4.0	—	—
6	Ca. of cervix	55	10.70	3.69	8.40	4.8	4.3	9.22	3.13	6.90	5.3	4.1	—	—
7	Ca. of cervix	69	10.44	4.03	6.57	6.0	4.8	8.65	4.38	4.65	5.4	4.7	—	—
9	Ca. of cervix, metastases	58	9.85	3.44	5.07	9.8	5.2	8.30	3.94	4.20	9.8	4.8	5.6	− 4.3
11	Ca. of cervix	26	11.00	4.13	7.56	3.9	4.7	—	—	—	3.5	—	—	—
12	Ca. of cervix	42	10.23	3.41	7.56	7.5	4.3	8.99	3.56	6.27	6.8	4.2	5.8	− 0.4
13	Ca. of uterus, ascites	65	10.40	3.75	6.12	7.0	5.0	8.80	3.88	4.68	6.8	4.8	4.8	− 2.8
14	Ca. of cervix, ? met. liver	68	11.10	3.94	6.42	22.9	5.2	9.21	3.78	5.16	17.4	4.8	5.4	+26.5
16	Ca. of cervix	49	10.45	3.72	6.57	11.3	4.8	8.96	3.77	4.95	9.0	4.8	—	+ 3.3
19	Ca. of cervix and ovary	44	9.00	3.22	4.44	6.5	5.0	7.80	3.25	3.60	7.0	4.8	6.0	+21.0
20	Ca. of cervix, vagina met.	70	9.61	3.22	5.61	4.0	4.8	7.55	3.30	4.23	3.9	4.3	5.3	+26.0
25	Malignant lymphoma	18	10.55	3.56	6.96	10.4	4.7	9.50	3.58	6.36	5.8	4.4	5.8	+ 7.0
26	Ca. of cervix	51	9.85	3.63	6.30	37.8	4.5	8.02	3.81	5.28	27.5	4.2	7.2	+ 6.0
27	Ad.-Ca. of uterus	63	9.80	2.44	6.48	31.2	4.2	8.73	2.50	5.34	26.1	4.4	4.8	+ 6.1
28	Ca. breast, met. axilla	50	9.82	2.25	7.20	11.1	4.2	8.30	2.46	5.40	7.8	4.2	6.5	−12.8
29	Ad.-Ca. of ovary	54	10.20	2.68	5.82	12.9	5.0	8.60	2.72	4.62	12.2	4.7	5.7	+16.0
30	Ca. of cervix	67	8.88	3.22	4.80	4.8	4.7	7.55	3.13	3.63	1.3	4.5	4.9	+ 8.0
31	Ca. of vagina	49	10.21	2.59	6.57	17.7	4.7	8.65	2.74	5.55	4.1	4.3	6.6	+ 4.0
33	Ad.-Ca. of omentum	64	9.68	2.61	4.56	27.6	5.3	—	—	—	15.8	—	6.2	+14.0
36	Ca. of vagina	69	10.08	3.41	6.00	17.1	4.9	8.80	3.56	4.98	12.4	4.7	5.2	+ 5.5
39	Ca. of cervix, vagina met.	48	9.90	3.81	6.48	8.3	4.5	8.75	3.93	5.58	7.8	4.4	7.4	− 1.0
41	Ca. of cervix	75	9.92	3.31	6.66	13.5	4.5	8.69	3.41	5.01	10.7	4.5	5.3	+42.0

TABLE II—CONT'D

42	Ca. of cx., hypertension	83	9.90	3.09	6.60	18.6	4.5	8.33	3.09	5.16	14.4	4.3	6.4	+11.0
44	Ca. of cervix	33	10.00	3.08	7.38	4.9	4.3	8.65	3.69	5.88	4.2	4.1	-	-
45	Ca. of cervix	43	10.30	3.60	7.44	8.3	4.3	8.30	3.94	6.42	5.9	3.8	6.0	+14.5
46	Ca. tube, met. ov. and ut.	57	9.90	4.38	5.22	8.7	5.1	8.12	4.10	4.38	7.5	4.6	5.0	- 1.9
47	Ca. of uterus	53	9.65	3.44	7.02	10.0	4.2	7.93	3.50	6.00	8.4	3.8	4.9	+ 5.0
49	Ca. vulva, met. glands	73	9.92	2.72	6.45	8.7	4.6	8.04	2.97	5.16	8.0	4.2	6.0	+ 1.0
50	Ca. of cervix	37	10.05	3.47	6.72	9.2	4.5	8.74	3.50	6.06	7.7	4.2	5.0	+13.4
51	Ca. of cervix	39	10.17	3.56	6.90	10.4	4.5	8.89	4.10	5.22	8.1	4.6	7.0	+ 4.2
54	Ca. of cervix, metastases	42	10.02	3.88	7.32	10.1	4.3	8.19	3.97	5.94	9.3	4.0	5.4	-13.6
56	Ca. of cervix, met. bladder	34	10.85	3.85	7.98	5.3	4.4	-	-	-	-	-	6.4	+ 8.0
57	Ad.-Ca. of ovary, met.	37	10.05	3.31	7.62	3.9	4.2	8.91	3.75	6.24	3.9	4.2	7.6	+ 6.0
58	Ad.-Ca. of cervix	36	9.84	3.75	5.28	9.0	5.1	8.57	3.81	4.08	9.3	4.9	5.6	+19.5
59	Ca. of cervix	43	10.40	3.31	6.72	12.6	4.7	8.70	3.34	4.74	11.7	4.7	5.0	+13.0
60	Ca. Cx, Paral. Agitans	58	9.83	3.47	6.66	8.6	4.5	8.42	3.63	5.28	10.5	4.3	6.4	+53.5
63	Ca. Cx., hypertension	57	10.50	3.88	6.69	3.3	4.8	8.73	3.81	5.37	3.2	4.4	6.5	+ 5.5
65	Ca. of cervix	67	10.10	4.28	7.26	8.3	4.4	8.80	4.44	5.94	8.1	4.3	5.3	+21.5
66	Ca. of cervix	37	10.70	3.19	6.60	11.6	4.9	8.83	3.30	5.55	7.2	4.4	4.8	+ 1.2
67	Ca. of cervix, metastases	58	10.85	3.56	7.32	10.7	4.7	9.16	3.47	6.24	11.3	4.3	6.7	+ 3.9
70	Ca. of cervix	30	10.45	3.77	7.05	11.7	4.6	9.04	3.91	6.09	10.5	4.4	4.4	+19.3
71	Ca. of cervix	47	11.35	3.55	7.80	10.2	4.7	9.48	3.55	6.54	9.6	4.3	6.5	- 8.4
72	Ca. of uterus	56	10.68	3.35	7.80	12.6	4.4	8.80	3.42	5.73	12.0	4.3	8.2	- 3.5
73	Ca. of uterus	64	10.95	2.98	7.08	9.9	4.8	9.03	3.58	5.46	9.3	4.6	7.6	+19.8
76	Ca. of cervix	56	9.66	4.31	7.74	8.7	4.0	8.08	4.44	6.18	10.8	3.8	6.4	+ 5.5
77	Ca. of cervix	77	9.50	4.19	6.42	9.9	4.4	7.92	4.69	4.92	10.2	4.2	6.8	- 1.6
	Average	52.9	10.15	3.44	6.65	10.6	4.63	8.59	3.54	5.38	9.04	4.38	5.94	+ 8.3

Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca^{++}) are expressed in mg. per 100 c.c., serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong[8] units, urine pH in units and basal metabolic rate (BMR) in per cent deviation from normal.

*Abbreviations used for diagnosis:

Ad.-Ca., adenocarcinoma; Ca., carcinoma; Cx., cervix; Ing., inguinal; Met., metastasis or metastatic; Ov., ovary; Paral., paralysis; Ut., uterus.

be the explanation, as they have not been excluded. However, with this in mind it is of interest to note that in the cancer group there are twelve other cases with definite evidence of metastases, to lymph glands, vagina, and omentum, all of which show normal phosphatase values.

TABLE III. SUMMARY OF RESULTS ON BLOOD AND BLISTER FLUID

	CANCEROUS			NONCANCEROUS		
	MIN.	MAX.	AVE.	MIN.	MAX.	AVE.
Serum						
Ca	8.88	11.35	10.15	9.60	11.03	10.27
P	2.00	4.38	3.44	2.50	4.41	3.40
Pr	4.56	8.40	6.55	4.23	8.10	6.99
Ph	3.3	37.8	10.65	3.9	21.6	7.52
Ca++	4.0	5.4	4.63	4.2	5.2	4.57
Blister Fluid						
Ca	7.55	9.50	8.59	7.90	9.30	8.77
P	1.81	4.69	3.54	2.53	4.41	3.58
Pr	3.60	6.90	5.38	3.54	6.45	5.77
Ph	1.3	27.5	9.04	3.6	20.2	6.94
Ca++	3.8	4.8	4.38	3.6	4.9	4.33
Urine pH	4.4	8.2	5.94	4.6	7.6	5.73
BMR	−13.6	+53.5	+8.3	−12.7	+30.0	+2.5

Calcium (Ca), inorganic phosphorus (P), and calcium ion concentrations (Ca++) are expressed in mg. per 100 c.c., serum protein (Pr) in gm. per 100 c.c., phosphatase (Ph) in King and Armstrong's units, urine pH in units and basal metabolic rate (BMR) in per cent deviation from normal.

Values for phosphatase in blister fluid correspond with those for blood but are lower than those for blood in nearly all cases. This indicates that the phosphatase enzyme is diffusible and in the rapid formation of blister fluid by diffusion of intracellular or blood fluids that phosphatase may be found in slightly lower concentrations than those present at the source.

The results of our basal metabolic rate determinations show nothing of interest. While the average figure for the cancer group is higher than the average for the noncancer group this is due to a larger number of high values in the former group. We feel that the number of variables here are too great, as evidenced by the range of − 12.7 per cent to + 30 per cent in the control group. Certainly no correlation can be established with malignancy per se. The highest value in the cancer group (+ 53.5 per cent) was obtained on a patient with paralysis agitans and malignancy. We have a few cholesterol determinations on cases of malignancy that confirm previous work[14] and would also indicate that there is no significant change in metabolic rate in cancer.

Similarly the variations of urinary pH in the two groups are so wide that the correspondence of the average figures will give little if any information as to the metabolic processes in either group. We had hoped to find a marked difference in the two groups, if there was a difference in metabolism of a cancerous and noncancerous individual. Our results show that urinary pH may be affected by so many

factors (e.g., dietary, respiratory, temperature, infections, etc.) that the determination is useless as a measure of acid base balance of the body. The one patient with pH 8.2 in Table II had a mild pyelitis.

SUMMARY

This second set of 50 female patients with malignancy and 26 without malignancy shows that no change in calcium or phosphorus metabolism is demonstrable in the blood or blister fluid of persons with cancer. Average protein figures for blood serum are slightly lower in the cancer group, and this will explain why the average calcium figures are slightly lower.

Calcium ion concentrations are normal in malignancy, as we have shown before.

Serum phosphatase is not changed by the malignant conditions here considered. In two patients out of the fifty, we have unexplained high values that may be due to the cancer itself. In another two patients with probable metastases to liver, we have found moderately raised values. In twelve cases of cancer with evident metastases to glands, omentum, or vagina, the serum phosphatase values are normal.

Basal metabolic rate in our cancer cases varies from -13.6 per cent to $+53.5$ per cent and in our control group from -12.7 per cent to $+30$ per cent. While average basal metabolism rate is higher for the cancer group, we do not think that this indicates a speeding up of metabolism by cancer.

The pH of a catheterized morning specimen of urine may vary from 4.6 to 7.6 in ward patients without pyelitis and from 4.4 to 8.2 in cancer cases. The difference in the group averages is not significant.

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AN EXPERIMENTAL STUDY OF DISSOLUTION AND ABSORPTION OF RETAINED DEAD FETUSES*

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INTRODUCTION

FETUSES killed experimentally and retained in utero offer an opportunity for study of autolytic processes which occur in an aseptic environment. The rates of these processes in different types of tissue can be compared and the sequence of degenerative changes determined. Such knowledge may have significance in the study of clinical cases in which spontaneous death has occurred. Ballantyne has emphasized that before one can rightly understand the pathology of the dead fetus a clear mental picture must be had of the gross and histologic appearance of the macerative changes. One must construct the common factor of maceration before he can differentiate the special changes due to individual disease in the fetus.

Two major types of material may be utilized in approaching this problem: first, chance specimens from clinical cases and those obtained from various animal dissections; second, material obtained by actual experimentation in which death of the fetus is caused by the investigator under conditions which may be more or less closely controlled. Cases in the first group usually have some pertinent data missing, which increases the difficulty of correct interpretation, a fact generally recognized by those working on such material (see Ballantyne, Greenhill, Meyer, Polak and Beres, Strachnan, Thomsen, and others). Studies on the second kind of material are decidedly few in number in spite of the fact it offers results of a more satisfactory nature (see Fraenkel, Koebner, Kuntz, and Corey).

It is difficult to construct a clear picture of the degenerative changes occurring in a fetus after death, in spite of the many published descriptions dealing with the condition of stillborn young and of dead fetuses retained in utero. Although discrepancies appear in the literature it does not necessarily follow that inaccurate observations were made. It is more probable that insufficient data were on hand. A good deal of the past work was based on specimens found dead in utero. Descriptions of this kind of material have been made for years.

The fault with such material lies in the incompleteness of data which may possibly be related to the dissolution of the fetuses. Such factors as cause of death; whether or not the fetus was normally developed when

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*Condensation of the original paper was dictated by lack of space; therefore many of the detailed findings have been omitted.

death occurred; length of retention after death; age of fetus when death occurred; disease and, possibly, the condition of the mother, all may have some effect upon the retrogressive changes. In nearly all the earlier work on fetal dissolution at least one, and generally two or three, of the above factors have been either uncontrolled or not taken into account.

In the present work every attempt has been made to avoid incompleteness or omission of the factors just mentioned. Even with all these precautions considerable unexplainable variation still appeared. However, the data obtained from studying this material are believed to be sufficiently uniform to indicate the general course followed by the retrogressive processes of various fetal structures.

MATERIALS AND METHODS

Young albino rat females were caused to retain one dead fetus. In each case, the fetus was the one nearest the fallopian tube, and it was killed on the fourteenth day after sperm were discovered in the vaginal smear. The operation to kill the fetus consisted in making a medial ventral abdominal incision to expose the uteri. A small incision was made in the uterus just at the periphery of the placenta of the fetus to be killed. A needle with the end bent to form a loop was inserted through this incision and rotated; thus the entire placenta could be freed by this form of curettage. Abortion was prevented by ligating the uterus. Abortion of the litter mates occurred in only two cases and was probably the result of undue mechanical manipulation of the uterus at the time of operation.

In all, 25 fetuses were retained dead in utero for the following periods of time; 12 hours, 1, 2, 3, 4, 8, 9, 11, 14, 15, 17, and 22 days. At the end of the allotted time the portion of uterus containing the dead fetus was removed, sectioned serially, and stained with Ehrlich's hematoxylin and eosin for histologic examination. One fetus of the litter was removed at the time of operation in most cases and fixed as a control.

To determine how soon the type of curettage employed kills the embryo, ten fetuses, from fourteen and fifteen days' gestation to older ones of nearly seventeen days, were treated by this method and taken out of the uterus within 20 to 60 minutes for examination under a dissecting microscope. In no case was the heart beating more than one hour after the operation.

OBSERVATIONS

Variation in degree of development reached by the fetuses was relatively large, although in every instance these fetuses were killed on the fourteenth day of gestation. The stage of development reached was determined primarily by the condition of the lungs, metanephros, and appearance of material around the notochord. The cases were separated into three groups, 12 being within the "mean" degree of development, 5 which might be called "underdeveloped," and 6 which might be classified as "advanced."

The general histologic condition of the entire fetus was determined in each case. Such items as the amount of necrosis, distortion of structures, and organization

of organs were used in making these determinations. As a result of such a study it was readily seen that variation in degree of dissolution occurred for a given length of retention. This agrees with some observations made by Corey.

It also appeared that the ''underdeveloped'' fetuses were in each case better preserved than those which were further developed yet retained for the same length of time. The fact the fetus is underdeveloped indicates it is progressing slowly, and when this development is stopped experimentally, death may not follow as promptly as in the case of a fast growing fetus. Stockard has shown in somewhat analogous situations that there is less immediate disturbance to the slower developing fetal material. This may explain why in the ''underdeveloped'' cases there is not as much disintegration in the same length of time.

Two rather distinct types of dissolution were found, which, because of their appearance, were termed ''loose'' and ''condensed.'' In eight instances the type of dissolution could be definitely termed ''loose'' and in five other instances ''condensed.''

The cellular material in the ''loose'' type appeared loosely held together. There were many small irregular spaces in the fetal tissues; the body cavities were not filled completely by the surrounding material; desquamation of the peripheral tissues generally occurred; this occasionally loosely filled the body cavities. As a result of this type of dissolution the uterine cavity after two weeks of retention contained necrotic débris made up of strips of membranes, small groups of cells and individual cells.

In the ''condensed'' type of degeneration the organs and structures ran together, filling the body cavities and resulting in a quite solidly packed mass of tissue. Identification of structures was very difficult in this type. After long retention the débris appeared similar to that of the ''loose'' type. Because of this similarity, separation of the two types was difficult after more than seventeen days' retention.

Determination of the type in progress could not be made until the fetus had been retained at least forty-five hours, nor, due to the slower rate of retrogression, could it be determined in some of the ''underdeveloped'' cases.

A careful histologic study was made of various fetal structures for each of the retention times previously mentioned. The structures studied were skin, capillaries, endothelium, heart, inner ear, eye, central nervous system, digestive tract, liver, kidneys, gonads, and sclerotome or precartilage. Such a study showed the progressive steps of dissolution resulting from increased length of retention after death and also indicated the respective comparative rates of retrogression existing between these structures.

Desquamation of the epithelium began within twenty-four hours and after seventy-two-hours retention was so extensive that it adhered to the fetus only in small areas.

The central nervous system showed some variation in appearance within the same retention times. It may be said, however, that distortion had begun within twelve hours, but it was not until after seventy-two hours that considerable collapse of the system was evident. Although the system was quite disorganized after seventy-two hours the cellular material stained fairly well. This reaction was poor by eleven days' retention. Identification was impossible after fourteen days. The spinal ganglia at first tend to be better preserved than the central nervous system but later, from eight days' retention on, appear similar in condition to the nervous system.

In the case of the eye, the retina appeared to undergo relatively the same processes as the brain and at approximately the same time. The lens underwent dissolution at a slightly more rapid rate than the retina (Fig. 1).

The inner ear underwent disintegration quite rapidly and karyorrhexis appeared to play a prominent rôle. Distortion occurred in cases retained twelve hours, and

by twenty-four hours the cellular organization was poor. This structure was not identified in cases retained longer than fourteen days (Fig. 2).

Distortion or folding of the epithelium of the digestive tract was not common even in cases of prolonged retention and when found occurred in the stomach. In some

Fig. 1.—Example of the dissolution of lens and retina in cases retained fourteen days.

Fig. 2.—The epithelium of the inner ear after eight days' retention.

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Indications of karyorrhexis were first noticed in the esophagus after eight days' retention, in the stomach after four days, and in the intestines after three days. This system could not be determined after two weeks' retention except in the "underdeveloped" cases, and even there it was in a poor state of preservation.

The liver was characterized by a gradual and progressive dissolution in direct ratio to the length of fetal retention. The periphery in most cases, retained forty-eight hours or longer, appeared to have been more greatly affected by the processes of dissolution than the more central areas. This was shown more strikingly, in some cases, in the area lying nearest the placenta. The arrangement of liver cells was somewhat disturbed after twelve hours' retention and after ninety-six hours considerable disorganization had occurred. By fourteen days' retention this organ was quite disorganized and could not be determined after this time except in the "underdeveloped" cases. The liver had started to spread out and lose its normal shape appearing to have become semifluid in consistency after twenty-four hours' retention. This process was quite advanced after ninety-six hours.
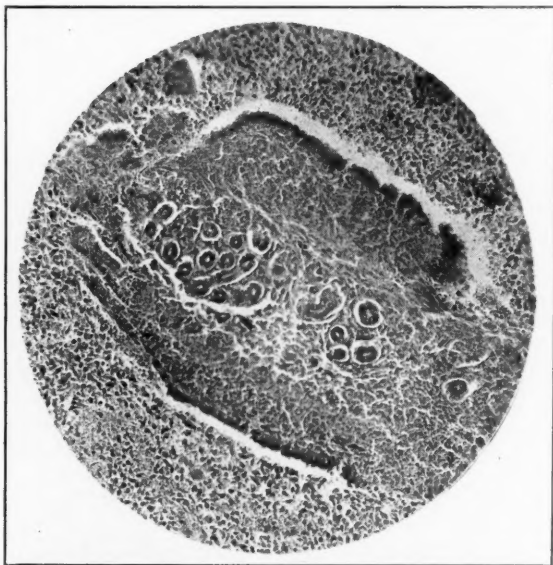
Fig. 3.—Metanephric tubules after being retained twenty-two days.

The general outlines of the kidney tubules persisted remarkably well even after relatively long retention. In the degenerative processes here the cells did not lose distinctiveness abruptly but gradually faded until no longer visible as individual entities. The nuclei began to display some karyorrhexis in the seventy-two- and ninety-six-hour cases. After fourteen days' retention no cell outlines were observable and the nuclei were very lightly stained. In one of the cases retained twenty-two days the kidney could be identified. The material was entirely necrotic but the general tubular arrangement could be seen (Fig. 3).

The endothelium, even after twelve hours' retention, had disappeared from practically all the capillaries, particularly those around the brain and in the dermis. In the larger vessels it had undergone desquamation after forty-eight or seventy-two hours. This was not true of the endocardium.

Very little loss of general organization occurred in the heart at any stage. Even when retained so long in some cases as to lose its affinity for stain the general arrangement, outline, and lumen persisted. After long retention periods the heart

chambers may break apart; yet even when this occurred the general organization of the tissue was relatively well preserved. The endocardium was nearly always present as a continuous lining, although it generally was raised from the underlying muscle. The heart took practically no stain after retention periods longer than fourteen days.

Very little distortion or loss of organization of the cartilage occurred even after long retention, although the nuclei developed irregularities in shape within seventy-two hours. The staining reaction was very poor after nine days' retention.

The relative degree of dissolution and preservation in various fetal structures was determined within the same fetus by histologic examination. Comparisons were made only with other structures of the same fetus. Such comparisons indicate whether or not a structure consistently displayed the same relative degree of dissolution in regard to the rest of the fetus.

The capillaries, epidermis, and inner ear were the most consistent in showing poor preservation. The liver was one of the structures more consistently showing better preservation. While the kidney tubules were quite well preserved in the majority of cases the ratio was not so high as in some of the other organs. They were, however, better preserved than the closely adjacent gonads. The heart, sclerotome, and precartilage were the best preserved of all the structures studied.

Three regions of the central nervous system were compared: brain, anterior cord, and posterior cord. The anterior cord was considered as that portion of the level dorsal to the lungs while the portion at the level of the cloaca was termed as posterior cord.

There were eighteen cases in each of which all three regions could be determined. It was found that the brain was better preserved than the other two regions in 1.85 per cent of the cases. That the anterior cord was better preserved in 7.40 per cent of the cases, while the posterior cord was better preserved than the other two regions in 22.22 per cent of cases. There were, however, 10 instances in which all three regions possessed the same degree of dissolution, or 55.55 per cent of the cases.

Thus, the data indicated that the central nervous system as a whole commonly underwent dissolution at the same rate. However, taking the length of retention into consideration, of the cases in which the degree of dissolution was comparable in the three regions, one-half had been retained for short periods of time. All the cases retained twelve or twenty-four hours, but one, were characterized by an equal degree of dissolution in the three regions.

The cases showing the same degree of dissolution in the three regions were also considered in respect to the general amount of disintegration of the fetus as a whole, and from this view, it appeared that usually these regions were the same in fetuses which were well preserved.

Thus it appeared that all but two of the cases in which the relative degree of dissolution was the same in the three regions of the central nervous system belong to one of the above two categories.

It appears from the foregoing that the three regions tend to be the same in fetuses retained for short periods or in those in which the disintegrative processes are not particularly advanced. This would indicate that the variation which occurred between these regions tends to arise after forty-eight hours' retention and in cases in which such variation occurred the posterior cord was more often the better preserved.

The digestive tract was divided into three regions: esophagus, stomach, and intestines. These were compared with each other in the same fetus in the same manner as was done with the central nervous system. The data thus obtained show the same general tendencies as the central nervous system, although the percentages were slightly different.

There was no actual correlation between the central nervous system and digestive tract in regard to the relative degree of dissolution. For example, cases in which the posterior cord showed little dissolution were not necessarily those in which the intestine was better preserved.

Comparatively, the central nervous system and digestive tract could not be said to belong to either the poorer or better preserved structures.

In the majority of cases the first reaction of the maternal white cells to the presence of dead material in the uterine cavity consisted in migration of polymorphonuclear leucocytes into that region. Later these decreased in number while the lymphocytes increased in number.

Cases in which fetuses were retained from twelve hours to four days showed more polymorphonuclear leucocytes in the uterine wall than cases of longer retention. Variation in numbers present ranged from nearly normal to very abundant, and leucocytes occurred in greatest numbers in cases of three- and four-day retention, particularly in the area of placental attachment. These elements could be traced, moreover, from engorged vessels in the uterine wall to the uterine cavity. Fetuses that had been retained the longest showed practically a normal condition in regard to these cells and gave no evidence of migration such as mentioned above.

Polymorphonuclear leucocytes found in the uterine cavity varied somewhat in number but were usually present in greater amount at about the period of eight or nine days' retention. Their occurrence was most frequent on the periphery of the placenta. Their number decreased in cases retained longer than this and by twenty-two-day retention practically none were present, although the uterine cavity contained considerable necrotic débris.

The lymphocytes began increasing about the time the polymorphonuclear forms had begun to diminish and reached greatest concentration in the uterine wall at eight to eleven days' retention and in the uterine cavity from nine to seventeen days. These elements rarely occurred in cases retained longer than seventeen days.

Numerically the lymphocytes were in no instance equal to the greatest number of polymorphonuclear leucocytes.

DISCUSSION

It must be kept in mind, in any attempt to correlate the present findings with those of previous workers, that earlier studies of this problem were carried out on several different types of animals and that such factors as stage of development of the fetuses, length of retention, and cause of death were not in every case clear. Therefore, great care and some mental reservation must be exercised in making comparisons. The results of the present experiments on fourteen-day rat fetuses, material which heretofore has not been used, are, therefore, not strictly comparable to most results reported in the literature.

There appears to be no questioning the fact that autolysis is the major process concerned with dissolution of dead fetuses. That liquefaction of dead tissue inside the body is actually brought about by intracellular enzymatic digestion was pointed out by Solkowski who named the process "auto-digestion." This process was renamed "autolysis" by Jacoby and established as occurring in retained dead fetuses by Schlesinger.

Thomsen and Polak and Beres found that in one to ten days the epidermis of still-births was raised up in the nature of "blebs" containing serum, and from ten to forty days it was peeling off or absent. A similar condition of "bleb" formation

was seen in the rat, but it occurred within twenty-four hours and at no time was as prominent as described by them.   Generally after forty-eight to seventy-two hours desquamation of the epidermis was so great that very little remained on the fetus. In the human being, Strachnan speaks of swelling of the superficial layers of the epithelium, as though these structures were taking up fluid, as one of the first changes in the epidermis.   A similar though not so pronounced condition was seen in the rat after twenty-four hours' retention.

With respect to changes in the central nervous system, no histologic description wholly comparable to the one previously given has been found in the literature.   Kuntz, in describing a condition in the cat, speaks of the lumen being more or less filled by fragmented cells and tissue débris, but very little was known concerning the history of the fetuses.   Somewhat similar conditions were noted in the rat after retention of seventy-two to ninety-six hours.

Polak and Beres mention an altering in shape of the liver through softening during the second stage of from ten to forty days.   Thomsen, on the contrary, in speaking of the same stage, claimed that the liver is noticeably soft but retains its shape until removed.   In the rat the liver had begun to lose its shape within twenty-four hours, and after forty-eight hours it had begun quite noticeably to spread out to fill the surrounding body cavity.

Greenhill, in describing the liver of a human fetus retained twenty weeks and undergoing mummification, noticed that degeneration was more marked in some areas than in others but did not localize these areas.   This point is of some interest as it was found in the rat after forty-eight hours' retention, the periphery of nearly all the livers displayed more advanced dissolution than the medial portions.   At present the question as to why there should be regional differences in the amount of degeneration of the same liver cannot be answered.   If only a straight autolytic process is involved, the assumption seems warranted that the dissolution should be the same throughout.   This condition, however, was not found.

The great variation in the relative amount of dissolution of the liver reported in the literature apparently results, to some extent, from the diverse ages of the specimens studied.   Adult livers or those of nearly full-term fetuses undergo rapid maceration while, as shown by the present work, those of fetuses of an earlier stage of gestation do not undergo rapid autolysis.   (See Mendel and Leavenworth, Jones and Austrian, Long and Parkes, Vernon, Wells, Thomsen, and Corey).

Thomsen, in describing the kidney, states that from one to ten days the convoluted tubules show marked blurring and the lumen contains detached material; the nuclei are either faintly stained or take no stain at all.   From ten to forty days there is widespread karyolysis in the cortex.   It must be taken into consideratioin that he was dealing with stillbirths; the author, on the other hand, was working on rats in which the metanephros was not as well developed.   With this qualification in mind it can be said that the present work did not confirm that of Thomsen's.   It appears that a considerable difference must occur between the degenerative processes in the kidney of nearly full-term fetuses and in those near the middle of gestation.

The endothelium of the smaller blood vessels disappeared very rapidly and was shortly followed by the disappearance of that of the larger vessels.   This is similar to the condition described by Kuntz for the cat.   He finds, however, the same condition true for the endothelium of the heart.   This finding was not confirmed; on the contrary, the endocardium persisted remarkably well even after long retention.

According to Mall the heart becomes more resistant than the other organs after the fifth week. This is the only reference found dealing with the comparative rate of dissolution in this structure. The present studies confirm his observations, for even when very few other structures can be identified, the heart retains its shape but generally stains lightly.

Various fetal structures were compared with each other in the same fetus in respect to the relative amount of dissolution. The variation between these structures depended upon the rate of the retrogressive changes; especially so since in these cases the processes began at practically the same time in each organ.

The structures studied are listed below in regard to the amount of dissolution, starting with those showing the greatest effects. It must be remembered, however, that this order is not invariably followed and that the list is, therefore, somewhat arbitrary: (1) capillaries, epidermis; (2) ear; (3) lens; (4) retina; (5) brain; (6) esophagus; (7) stomach; (8) gonads, anterior spinal cord, metanephros; (9) posterior spinal cord; (10) intestines, liver; (11) sclerotome, heart; (12) precartilage.

The problem as to what effect the stage of development has upon the dissolution of retained dead fetuses does not appear to be settled at present. Needham states the situation by saying the younger the fetus the more complete the removal and no question arises as to the accuracy of this. In the human being, both Pigeaud and Thomsen point out that in the first stages of development or in premature fetuses maceration is more rapid than in cases of full term. It is difficult to see how this is brought about in view of the work of Vernon, Jones and Austrian, and Mendel and Leavenworth. They agree that as fetal life progresses enzyme activity becomes increasingly effective. If this factor is taken into consideration, autolysis should proceed more slowly in fetuses which have had a retarded development. This is in accordance with the data on hand.

There appears at present no correlation between the "loose" and "condensed" types of dissolution and the rate of disintegration, since the latter is approximately the same in both cases.

The "condensed" type appears to have had its fluids extracted, resulting in the cells of the entire fetus lying compactly together with practically no intercellular spaces or body cavities. This process is not similar to mummification and the only report seen which describes something resembling it is that of Koebner, who speaks of a "dry retrogression" in which the fetal tissues run together and identification of structures is very uncertain.

The "loose" type is the more common and conforms to the general descriptions of macerating fetuses.

The definite causes underlying these two types of dissolution are as yet undetermined. As far as is known the experimental procedure was the same throughout.

In the present work, nuclei could be seen in cases of over two weeks' retention. This does not support Well's statement that fetuses which have undergone aseptic autolysis in the uterus show a complete loss of nuclei in five or six days.

There appears to be some contradictory evidence as to the chemotactic influence exerted on leucocytes by dead material. Bradley, in discussing dead tissue in the body, states that phagocytosis is secondary to autolysis, occurring after the tissue is broken down and some substance formed which sets up a chemotactic attraction. Amino acids are a part of the end products of autolysis, and Wolf found that such acids are positively chemotactic to a certain extent. However, Wells states that chemotactic substances do not seem to be formed in aseptic dead tissues and that the absence of leucocytic infiltration is so marked that it seems possible that substances with negative chemotactic effect are present.

In the present work, leucocytic migration to the uterine cavity did occur to some extent in cases of shorter retention but was negligible in fetuses retained for longer periods of time. In event of migration, concentration of leucocytes was greatest on the periphery of the placenta and consisted mainly of polymorphonuclear cells. It would thus seem that these appeared in response to either the mechanical injury to the uterine wall and placenta or to some influence exerted by the dead placenta. However, their presence was of short duration, for after eight or nine days very few were found although the placenta was still present.

In cases of longer retention the uterus contained a good deal of necrotic and presumably autolyzing material. There were no polymorphonuclear leucocytes, yet this material was not enclosed by intact membranes and was therefore free to exert a chemotactic attraction for polymorphonuclear leucocytes, which is in agreement with Well's above observation. It appeared, moreover, that only a slight attraction for lymphocytes developed.

Few investigators working on dead fetuses have paid attention to the time at which autolytic processes are initiated. Kuntz and Corey, in studying fetuses retained dead in the uterus, concluded that considerable time must elapse before the processes became apparent. Long and Parkes, however, found that changes could be seen after incubating rat, mouse, and pig fetuses in Ringer's and under toluene for thirty-four hours. Nicholas, on the other hand, placing eight- to nine-day rat fetuses with undisturbed embryonic membranes in Ringer's and Locke's physiologic saline at body temperature for at least six hours, found no changes occurred, but after twelve hours considerable disintegration was in evidence.

Disintegrative changes had begun in the fetuses studied in the present work after twelve hours' retention in utero. Such changes, although not considerable, were, nevertheless, quite definite. It thus appears that the data on initiation of autolytic processes appearing in this report agree fairly closely with those of Nicholas on incubated fetuses.

According to Long and Parkes and Corey the liver and gastrointestinal tract are the first to show the effects of macerative or disintegrative processes, and Corey further states that the changes spread from these structures to the other organs. This is not confirmed by the present work. All the fetal structures of cases retained twelve hours appeared to be practically the same in respect to retrogressive changes, with the possible exception of the dermis, ear, and capillaries. Thus, it would seem that the autolytic processes had begun in the various structures of these fetuses at practically the same time and did not spread from some more or less localized point as indicated by Corey. It should be kept in mind, however, that the present work was done on fourteen-day fetuses whereas Corey worked on those near full term, and hence the two lots of material are not strictly comparable.

Although there is contradictory evidence as to the time and place autolysis is initiated, there appears to be a uniformity of opinion that it proceeds at different rates in different structures. While it is generally accepted that the rates vary, not all workers agree as to the amount of variation nor as to the structures showing it. It should be pointed out that in the present work the retrogressive changes at first appeared to be synchronous in the fetal structures and that differences in amount of dissolution occur secondarily.

It is interesting to note the excellent condition of the females carrying a dead fetus. They not only nursed litters in a perfectly normal manner but would come into estrus, characteristic of the unoperated female after removal of her litter. This behavior was typical even though a dead fetus was being carried in one horn of the uterus.

Appearance of estrous changes in the vaginal smears suggested the possibility that these females could become pregnant while still absorbing a dead fetus in one uterine horn. This was confirmed in the one case tested, pregnancy resulting in a litter of two. Of interest in this connection is a case reported by Løvset and one by Thoms, in the human being, in which a female became pregnant while the uterus contained a dead fetus.

SUMMARY

1. An experimental method is described for the study of retrogressive changes in retained dead fetuses in the rat.

2. The initiation of retrogressive changes in the dead fetus occurs early, within twelve hours.

3. The respective rates of dissolution of most of the formed elements of the fetus are uniform up to twenty-four hours' retention, after which time variation becomes apparent.

4. Aside from described exceptions, the fetal structures in fourteen-day rat embryos can be enumerated as follows, starting with those showing the greatest amount of dissolution: (a) capillaries, epidermis; (b) ear; (c) lens; (d) retina; (e) brain; (f) esophagus; (g) stomach; (h) gonads, anterior spinal cord, metanephros; (i) posterior spinal cord; (j) intestines, liver; (k) sclerotome, heart; (l) precartilage.

5. Two types of dissolution are described as quite apparent in the early stages of retention; ''loose'' and ''condensed.'' In later stages the distinctive characteristics of these two types become gradually obscured.

6. Evidence is offered of a chemotactic influence of the retained material toward leucocytes of maternal origin during the early stages of retention. This chemotaxis is not apparent in later stages.

7. It is possible for a female to become pregnant and to produce normal young while retaining a dead fetus.

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The author ligated the uterine tubes of rabbits with silk and with fresh aponeurotic sutures. He killed the animals at periods varying from one to seven months and found that within the first thirty days the lumen of the tubes was found completely obliterated at the site of ligation. However, in those sacrificed after thirty days, canalization of the tubes had been reestablished.

AUGUST F. DARO.

A BIOLOGIC TEST FOR THE DIAGNOSIS OF INTRAUTERINE FETAL DEATH*

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THE diagnosis of intrauterine fetal death is difficult, especially before the fifth month of gestation. Horner[1] has shown the x-ray is of no value before the fifth month because osseous development is slight. After osseous development is demonstrable by the x-ray, according to the work of Matthews,[2] and Stein and Arens,[3] the fetus usually must be dead from four to five days before enough degeneration of the brain tissue takes place to cause overlapping of the skull bones or asymmetry of the head, and ten to fourteen days are usually required for collapse of the thoracic cavity and horseshoe curvature of the spine. They have also shown that decalcification of the bones is not a reliable sign of fetal death, as errors in technic may give similar light areas. Since overlapping of the skull bones may occur during labor or with engagement of the head, it is not a very reliable sign. Falls[4] has shown that fetal heart tones may be heard with the vaginal stethoscope as early as the fourth month, and if after this stage of gestation heart tones or fetal movements cannot be heard, he considers this strong presumptive evidence of fetal death.

The object of this paper is to set forth our experience in the diagnosis of intrauterine fetal death, using the Schneider[5] modification of the Aschheim-Zondek reaction. The value of a test of this type is especially great in the early months of gestation, and in the later months of gestation, the reaction can be obtained twenty-four to forty-eight hours after the death of the fetus.

TECHNIC

Ten cubic centimeters of a fresh voided morning specimen of urine are filtered and injected into the marginal vein of the ear of a thirteen- to fifteen-week-old-virgin female rabbit, weighing between 4 and 5 pounds. From forty to forty-eight hours after injection of the urine, the rabbit is sacrificed and autopsied. Upon gross inspection of the rabbit ovaries, various reactions may be seen. It is advisable to examine the ovaries immediately after killing the rabbit before postmortem changes have set in. If the ovaries are opaque, cylindrical, and flat with no mature follicles, they are too immature to respond to the hormonal stimulus of the urine, and the test

should be repeated. If the ovaries are rounded and contain one or more mature follicles that contain no hemorrhage, the test is negative. Should the follicles contain peripheral hemorrhage as shown in Figs. 1 and 2, the diagnosis of intrauterine fetal death may be made. One cannot differentiate by this method between retained placental tissue with the fetus expelled and the dead fetus still in utero. The same reaction is found whether a dead fetus or chorionic villi are in the tube, abdomen, or uterus. This reaction we have termed the dead fetus reaction. If the follicles are hemorrhagic throughout, the test is positive (Fig. 3).

In order to facilitate description of the cases in which the dead fetus reaction was obtained by using the above-mentioned method, the cases have been divided into seven groups. All the patients in each group have similar histories and physical findings.
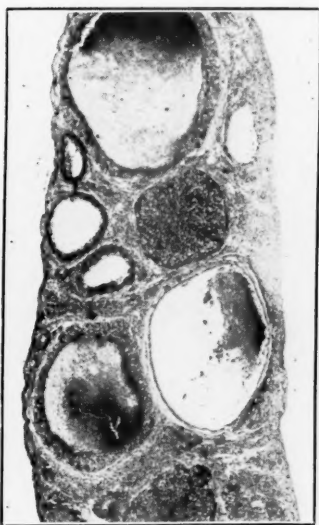
Fig. 1.   Fig. 2.   Fig. 3.

Fig. 1.—Drawing of an ovary from a dead fetus reaction, showing peripheral hemorrhage in the follicle.

Fig. 2.—Microphotograph showing peripheral hemorrhage in the follicle.

Fig. 3.—Drawing of positive reaction showing hemorrhage throughout the follicle.

1. In Group 1 the following case history is characteristic of the group:

CASE 1.—H. N., white, female, thirty-two years of age, grav. i, para 0, who had menstruated regularly until July 24, 1933, when she missed her period. She took large doses of castor oil and quinine early in August and three weeks later began to bleed vaginally. A rabbit was injected in the usual manner and a dead fetus reaction obtained. A diagnosis of incomplete abortion was made and the patient was curetted. Curettage revealed some degenerated placental tissue.

We had 18 similar cases in which, in an effort to produce an abortion, the patient took castor oil and quinine or some ergot derivative and succeeded in producing an incomplete abortion. The pregnancy

was proved by findings on curetting the uterus. In each case the dead fetus reaction was obtained before completion of the abortion, and in all cases we were able to find placental tissue in the clots passed on after curettage.

2. Group 2 is best described by the following case:

CASE 2.—Ko., aged twenty-four years, para i, grav. ii, was observed seventy-two days after the first day of her last menstrual period. The uterus had not increased in size after eight weeks of gestation. No bleeding or signs of fetal death were present. A rabbit was injected in the usual manner, and a dead fetus reaction was obtained. A dilatation and curettage were done, and degenerated placental tissue was found.

We have had 8 similar cases all giving the same results, 2 occurring in the first trimester of pregnancy and 6 occurring in the second trimester.

3. In the third group there are 15 cases in which urine was taken from the bladder by catheter on the delivery table after the patient had delivered a macerated stillborn child, and 10 c.c. was injected into a rabbit. In all these cases patients entered the hospital in labor and gestation varied from the fifth month to term. In all cases a dead fetus reaction was obtained. This was done in order to determine the reliability of the reaction in cases with a known dead fetus.

4. In Group 4 we have all patients who entered the Research and Educational Hospital with a diagnosis of threatened abortion.

It is a routine procedure at the Research and Educational Hospital to run a Schneider modification of the Aschheim-Zondek tests on all patients entering the hospital with the diagnosis of threatened abortion to determine whether or not there is a live fetus in utero. Efforts are made to retain the fetus in utero until a reading of the rabbit ovaries can be made. If the test shows the dead fetus reaction, sedative therapy is stopped, and the patient is allowed to abort. We have had 23 dead fetus reactions in these tests and each expelled macerated fetus or placental remnants twenty-four to seventy-two hours after therapy was stopped, 15 occurring in the first trimester of pregnancy and 8 in the second trimester.

5. Group 5 is the ectopic gestation group, and the following case history is characteristic:

CASE 3.—Br., twenty-five years of age, para ii, grav. iii, entered the hospital complaining of pains in the right lower quadrant of five days' duration. Slight enlargement of the right tube was found upon bimanual examination. Forty-two days had lapsed since the first day of the last menstrual period. An injected rabbit revealed a dead fetus reaction. A laparotomy was done and decidual tissue, but no fetus, was found in the right tube. There have been ten other cases with similar histories, similar findings on bimanual examination and all gave the dead fetus reaction. At operation all had placental tissue in one of the tubes.

6. In Group 6 we have patients who entered the hospital for treatment of eclamptogenic toxemia. At the time of their admittance the fetal heart tones were audible but disappeared later. The following case best illustrates this group:

CASE 4.—M. H., aged twenty-nine years, grav. v, para iii, seven months' gestation, entered the hospital with preeclamptic toxemia. The blood pressure was 200/130, 4-plus albumin, and many casts and red cells were found in the urine, and the phenolsulphonephthalein test showed 0 per cent at the end of two hours. The fetal heart tones were heard upon entrance to the hospital, but two days later disappeared. A rabbit was injected with the patient's urine in the manner described and autopsied forty-eight hours later. A dead fetus reaction was obtained. The patient went into labor four days later and delivered a somewhat macerated fetus. There were 4 patients in the group and all in the last trimester of pregnancy.

7. In Group 7 there are included the patients who had several tests run at intervals varying from two to seven days. In each case the fetus was retained in utero for longer than a week and all occurred in the last trimester. The following history is quite typical of the group:

CASE 5.—V. B., para i, grav. ii, entered the hospital on Oct. 10, 1934, with a diagnosis of preeclamptic toxemia. Examination revealed a colored female in the ninth lunar month of gestation, with a blood pressure of 200/110, a phenolsulphonephthalein of 50 per cent at the end of two hours, fetal heart tones 132, and a 3-plus Kahn test. The fetal heart tones were heard daily until November 10, when they were not heard. A rabbit was injected on November 11, 13, 15, 18, 20, and 23. The test at each time showed a dead fetus reaction except on the eighteenth when it showed a distinct positive. Here we had a false positive.

In all cases the pregnancy was terminated by the expulsion of a badly macerated fetus. In this group there were 4 cases. One had 3 tests over a period of ten days, another 3 over twelve days, another 4 over a period of fifteen days. The fourth case has been described. There was only one false reaction in this group.

The next 3 cases do not fall into any of the 7 groups but each has a special point of interest.

CASE 6.—E. McB. delivered a normal child but failed to expel the placenta. Manual removal was thought inadvisable, and the patient was put to bed with the placenta in utero. Rabbits were injected with 10 c.c. of urine on the seventh, eleventh, eighteenth, twenty-sixth, and thirty-second postpartum days. The test on the seventh, eleventh, eighteenth, and twenty-sixth days showed a dead fetus reaction. The test done on the thirty-second day showed a negative reaction. On the twenty-fifth day a small piece of grayish tissue was expelled and was found to be degenerating placental tissue. On the thirty-second postpartum day a sterile vaginal examination was done and no evidence of placental tissue was found. From the seventh to the thirty-fifth postpartum day, the patient had temperature varying between 100° to 106.4°. It was assumed that all the placental tissue was either absorbed or expelled between the test taken on the twenty-sixth and the third-second postpartum days.

CASE 7.—Ko., para i, grav. ii, aged twenty-six years, forty-one days after the first day of her last menstrual period, began to bleed vaginally and this bleeding

continued for two days. A rabbit was injected to determine whether or not the fetus was alive. A dead fetus reaction was obtained, but because the clinical history was more in keeping with a live pregnancy, a conservative attitude was taken. Two weeks after the first test a second was done and this time it was positive. The patient went to term and delivered. In this case we have a false dead fetus reaction where the fetus was alive.

CASE 8.—Hi., aged thirty-two years, para i, grav. iii, was obserevd in the thirty-second week of her gestation. Fetal heart tones were not heard after this time. X-ray picture of the fetus in utero did not show characteristic overlapping of the skull bones or any evidence upon which one could diagnose a dead fetus. A rabbit was injected in the usual manner and a dead fetus reaction was obtained. The patient failed to go into labor following two attempts at induction with the Watson technic. A Voorhees' bag was inserted into the cervix; the patient went into labor and delivered a macerated fetus four days after the dead fetus reaction.

Jeffcoat[6] of England reported a series of 9 cases similar to this series, using mice instead of rabbits. In his series he was able to predict termination of the pregnancy by the expulsion of a dead fetus 7 times. He, however, believed the reaction observed was due to an upset in the hormonal balance, there being a relative excess of estrin over prolan A and prolan B. He also thought the reaction was not indicative of fetal death but of an impending abortion due to the hormone imbalance.

Tate[7] using rats confirmed Jeffcoat's observations with a series of 7 cases with 6 accurate results. Jeffcoat's belief that the reaction was due to impending abortion rather than fetal death is not substantiated by this work. All his cases occurred early in pregnancy when a diagnosis of fetal death is difficult.

In our work in cases of premature labor, where the pregnancy was far enough along to hear fetal heart tones, we were unable to obtain a dead fetus reaction as long as fetal heart tones were audible, but twenty-four to forty-eight hours after the fetal heart tones disappeared the dead fetus reaction was obtained. This, plus the macerated condition of the fetuses upon expulsion and the fact the retained placental alone can give the reaction, has led us to believe that this is the result of fetal death rather than of impending abortion. From our work we are unable to state the causative factors for this reaction.

Bishop[8] has come to the conclusion that pregnancy tests depend on the presence or absence of functional chorionic tissue and not upon the life or death of the ovum. In our work we have occasionally observed positive Aschheim-Zondek reactions where there were no functioning chorionic villi. They have been observed in teratomas of the ovary and testes, dermoid cysts of the ovary, and serous cysts of the ovary.

To rule out the possibility of a fading reaction, the urine of 5 women postpartum was injected into rabbits, and all the reactions observed were either negative or positive and none yielded the dead fetus reaction. The reaction became negative twenty-four to seventy-two hours after the birth of the fetus. Dilution of the urine of 5 pregnant women was also tried, but here again the results were negative or positive. A positive reaction was observed with as little as 1 c.c. of urine and negatives with as much as 5 c.c. of urine, using the same technic.

CONCLUSIONS

1. Using the Schneider modification of the Aschheim-Zondek test, we have been able to obtain the dead fetus reaction with an accuracy of 95.3 per cent in a series of 86 cases.

2. The test is positive for dead fetus reaction as long as living chorionic tissue is in contact with the maternal blood.

3. Its value in ectopic pregnancy lies in establishing the fact of fetal death and, inasmuch as further growth is then arrested, affording information that the danger of rupture or abortion is decreased.

4. The reaction is not positive when postpartum or diluted antepartum urine is used for the test.

5. While not infallible, it is extremely valuable and should be used in conjunction with the clinical reactions in determining treatment in a given case.

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1817 W. POLK STREET

DISCUSSION

DR. A. E. KANTER.—This study is of interest, particularly in its reference to the work I have been trying to do on fish. We believe that the reaction in the fish test is the effect of the estrogenic agent, which does not decrease in the urine as quickly as does the prolan. We have had seven negative Friedman tests and seven positives in fish in cases proved at operation to be ectopic pregnancy.

If the test follows the same rule as it does in the fish, I am quite sure we are safe in saying that it is the estrogenic content which brings down the ovipositor and gives the findings Rezek described.

DR. REZEK (closing).—The test I have described will be valuable, particularly in cases of ectopic pregnancy to indicate which should be operated upon immediately and which could be treated conservatively. So far one patient has been treated conservatively. From a bimanual examination and history of this dispensary patient, a diagnosis of ectopic pregnancy was made and surgery was suggested, but the patient refused. We obtained a urine specimen and a dead fetus reaction was noted. Five tests in all were run, the last being negative. We have no proof that this patient had an ectopic pregnancy, because she was not operated upon, but there was good clinical evidence on which to base a diagnosis of ectopic pregnancy.

CARCINOMA OF THE BODY OF THE UTERUS*

A Review of 279 Cases With Five-Year End-Results in 211 Cases

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CARCINOMA of the fundus of the uterus is a frequent and highly malignant neoplasm. Within the last few years many statistical studies based on the value of different methods of treatment and of diagnosis have appeared. The following study was undertaken in an endeavor to check the results in our own series of cases.

MATERIAL

From Jan. 1, 1900, to Jan. 1, 1935, 279 patients suffering from carcinoma of the body of the uterus were admitted to the Hospital of the University of Pennsylvania. In this entire group the diagnosis was verified by histologic examination. Of the 279 patients, 211 were admitted five or more years before 1935, and these form the basis for the five-year, end-result investigations. In this group of 211 patients 5 are included in whom it was impossible to determine whether the carcinoma had its origin in the uterus or in the ovary. In view of the fact that a number of the old case histories were incomplete, some discrepancy in the number of cases will be noted in the various groups. Of the 211 patients admitted five or more years ago, 171 (81.0 per cent) have been followed and the results noted. All untraced patients are regarded as having died of carcinoma.

Age on Admission.—Table I shows the age on admission in 268 cases. Although carcinoma of the fundus may occur at any age, in our series the greatest number of

TABLE I. AGE ON ADMISSION FOR TREATMENT

AGE IN YEARS	PATIENTS	
	NUMBER	PER CENT
20-29	4	1.5
30-39	18	6.7
40-49	49	18.3
50-59	124	46.3
60-69	57	21.3
70-79	16	5.9
Total	268	100.0

patients, 124 (46.3 per cent), were between the age of fifty and fifty-nine. The youngest patient was twenty and the oldest seventy-six. Twenty-two patients (8.2 per cent) were under forty years of age.

*Read at a meeting of the Brooklyn Gynecological Society, March 6, 1936.

Menopausal Status.—Carcinoma of the fundus is often considered a postmenopausal disease, but of our cases, 80 patients (30.5 per cent) were in the premenopausal age as compared to 182 (69.5 per cent) in the postmenopausal age.

The Relation of Frequency of Childbearing to the Development of Fundal Carcinoma.—An analysis of the marital status showed that 223 patients were married and 55 were unmarried. In one, the status was not mentioned in the history. Of the 223 married patients, 150 (67.3 per cent) had undergone one or more full-term deliveries, whereas 48 (21.5 per cent) were nulliparous, and in 25 (11.2 per cent), parity was not known.

TABLE II. FREQUENCY OF CHILDBEARING IN RELATION TO DEVELOPMENT OF FUNDAL CARCINOMA

PREGNANCIES	PATIENTS	
	NUMBER	PER CENT
0	48	24.2
1	32	16.2
2	32	16.2
3	34	17.1
4	19	9.6
5	33	16.7
Total	198	100.0

Table II exhibits the number of full-term pregnancies in the 198 cases. In this series of cases parity played but a small part as a predisposing factor in the development of the carcinoma. The condition was relatively about as prevalent in those who had borne children as in those who had not. Nor was the number of children borne to each patient significant.

Chief Symptoms.—Metrorrhagia is undoubtedly the most important symptom of carcinoma of the uterine fundus. Although this type of bleeding may be the result of a benign condition, its presence demands immediate investigation in all cases. Hemorrhage was the first symptom observed in 80.5 per cent of the patients, and leucorrhea was noted in 10.3 per cent. The onset of bleeding and leucorrhea occurred simultaneously in 8 per cent of the patients. In 72.9 per cent of the patients the bleeding was predominantly of the intermenstrual type and was the most prominent symptom. In only 17.9 per cent was the metrorrhagia associated with menorrhagia, whereas menorrhagia alone was present in 6.8 per cent.

In the metrorrhagia the flow was usually scanty at the onset, but in a majority of patients it soon became moderate or profuse. In 30.9 per cent of the patients the bleeding was associated with a leucorrheal discharge. This was slight at the onset, but later became more profuse, foul, and in many of the cases irritating.

Although many of the patients comprising this series were in the advanced stage of the disease, only 58 (22.1 per cent) complained of pain.

Duration of Symptoms.—The average duration of symptoms prior to the onset of treatment was 17.9 months. In those patients who were still menstruating, the average duration of symptoms was 22.2 months as compared with sixteen months in the postmenopausal cases. Table III gives the duration of symptoms.

TABLE III. DURATION OF SYMPTOMS BEFORE BEGINNING OF TREATMENT

DURATION OF SYMPTOMS IN MONTHS	PATIENTS	
	NUMBER	PER CENT
Less than 12	113	43.8
12-23	75	29.1
24-35	13	5.0
Over 35	57	22.1
Total	258	100.0

Only 113 (43.8 per cent) of the patients sought treatment prior to one year after the onset of symptoms. In 96 cases the carcinomas were associated with myomas, and in this group the average duration of symptoms was 21.8 months, or 3.9 months longer than the duration of symptoms for the whole series. It was also observed that in those patients with myomas who had passed the menopause the duration of symptoms was nineteen months, as compared to sixteen months for the post-menopausal group in the whole series. Furthermore, the patients in the active child-bearing period who had associated myomas, the average duration of symptoms was 28.1 months as compared to 22.2 months for the patients in the entire series.

The association of myomas increases the difficulty of determining the presence of fundal carcinoma, and in our series it seemed to result in delay in seeking medical advice.

TABLE IV. ACCURACY OF PREOPERATIVE DIAGNOSIS

DIAGNOSIS	PATIENTS	
	NUMBER	PER CENT
Positive	184	67.9
Suspected	45	16.6
Unsuspected	42	15.5
Total	271	100.0

Preoperative Diagnosis.—Thus in 87 cases the diagnosis was actually dependent upon histologic examination, and in 42 of these the presence of a malignant neoplasm was unsuspected.

It is worthy of note that in the unsuspected group, 16 of the 42 cases of carcinoma developed in myomatous uteri, thus emphasizing the frequent association of these two neoplasms and also the increased difficulty of arriving at an accurate diagnosis in this type of case. The fact that nearly one-third of the cases in this entire group were not recognized prior to operation, and that 15 per cent of them were totally unsuspected until a microscopic examination had been made, shows the necessity for making routine histologic studies of all specimens of endometrium removed by curettage. It must be stated here that carcinoma of the fundus can never be recognized with certainty until the uterus is available for macroscopic inspection or until histologic examination of curettings can be performed. Cases that occur before or during the menopause or that are associated with uterine myomas are especially likely to give rise to confusion. Furthermore, the earlier the stage of advancement, the less positive is the preoperative diagnosis, and the greater is the likelihood of securing a permanent cure, provided the correct diagnosis is arrived at and treatment instituted.

Our studies also demonstrate the importance, in all cases of supravaginal hysterectomy, for supposed benign conditions of making an inspection of the endometrial cavity before closing the abdomen.

In cases in which the macroscopic diagnosis is in doubt, a frozen section should be examined before the abdomen is closed, so that the surgeon may perform a complete operation if carcinoma is found to be present.

The Reliability of Histologic Diagnosis.—If a sufficient amount of material is available for study, the histologic diagnosis should be correct in almost 100 per cent of the cases.

Paraffin sections of curettings may be prepared and made ready for histologic examination in twelve hours; these form the most satisfactory method of histologic examination for routine employment. When the curettings are abundant and an immediate hysterectomy is contemplated, one or more large pieces of tissue may be cut by frozen section. If the examination of the frozen section is positive for carcinoma, the diagnosis of malignancy may be accepted; if, however, the result

is negative, all the remaining tissue, including the remains of the frozen section block, should be cut by the paraffin method before carcinoma is excluded. When only a small amount of tissue is available, or when the tissue is secured in small particles, frozen sections are not satisfactory. When cutting paraffin blocks, it is important to cut at different levels in order that a particle of each piece of tissue may be available for histologic examination.

In the Laboratory of Obstetric and Gynecologic Pathology at the Hospital of the University of Pennsylvania no case during the last thirty-six years was diagnosed as carcinoma as the result of examination of the curettings that did not, when the uterus was subsequently removed, confirm the original diagnosis. Likewise, so far as we know, no case that was originally diagnosed as benign was later shown to be malignant. These statements are made in order to show that the histologic diagnosis of carcinoma of the fundus based on the examination of curettings is, when made under good conditions, reliable. It is needless to emphasize the hazards that may result from inexperience on the part of the pathologist, and it should be stressed that a histologic diagnosis based on the examination of curettings requires special knowledge and training.

Associated Pathology and Metastases.—Perhaps the outstanding feature in this series of carcinomas was the high proportion of cases found to be associated with uterine myomas, 34.9 per cent (96 cases). Other things being equal, it may be assumed that in those cases associated with myomas the prognosis would be better because of the increased thickness of the uterine wall, as the integrity of the myometrium is generally regarded as the chief feature on which to base the prognosis. However, probably the greater difficulty of diagnosis and the increased hazards of operation counterbalance this theoretic advantage.

Metastasis, or transtubal involvement of one or both ovaries, was present in 19 cases: the right ovary was involved in 3, the left in 6, and both ovaries were affected in 10 specimens.

The tubes were the seat of metastases or extension in 5 patients. In 8 instances, the omentum, intestines, epiploic appendages, mesosalpinx, or pelvic lymph glands were known to have been invaded.

In 15 patients extension to the parametrium was present on admission.

Sampson believes that transtubal implants occur, and as an initial step in all hysterectomies which are to be performed for known or suspected cases of fundal carcinoma, he has recommended the ligation of the tubes in the region of the ampulla in order to prevent any invasion of the abdominal cavity.

TREATMENT

It will be realized that in attempting to analyze the end-results secured in a group of cases that extend back over a period of thirty-five years many difficulties will be encountered, not the least of which are the various methods and modifications of treatment that may have been utilized. During the period covered by this analysis neither preliminary irradiation nor postoperative roentgen ray therapy was used routinely in the treatment of these cases. For comparison the cases may be divided into two main groups, namely: (1) Those treated by hysterectomy and (2) those treated by radium.

Of the 211 patients, all but 7 received treatment; four of the latter were believed too far advanced and three refused treatment. All the patients that were considered too advanced for treatment were seen prior to 1910 with exception of one patient. Today these would probably be given the advantages of irradiation either by

means of radium or roentgen ray or both. Previous to 1930 our radium dosage was not standardized, and often did not average over 2,400 or at most 3,000 mg. hours with a screening of either 2 mm. of aluminum, or brass or 0.5 mm. of platinum. Today as a minimum we use 4,800 mg. hours of radium with a screening of 1 mm. of platinum and 2 mm. of rubber, followed by deep roentgen ray therapy.

OPERATIVE MORTALITY

Under this heading are included all deaths that occurred in the hospital following treatment. Table V shows the mortality.

TABLE V. OPERATIVE MORTALITY

METHOD OF TREATMENT	PATIENTS		
	NUMBER	OPERATIVE DEATHS	
		NUMBER	PER CENT
Hysterectomy	115	5	4.3
Radium	89	2	2.2

Operative mortality for combined series, 3.4 per cent.

The five deaths that followed hysterectomy were all due to peritonitis. One of the deaths in the radium series was due to cardiac failure and occurred within a few hours after treatment; the other death was due to peritonitis. It is questionable whether either of these deaths should be attributed to the irradiation. Furthermore, in considering the mortality it should be remembered that the routine treatment consisted of hysterectomy, and that radium irradiation was generally employed only when some contraindication to the performance of hysterectomy was present, so that the group treated by radium irradiation practically consisted of all the bad risks in the entire series.

FIVE-YEAR SALVAGE

For purposes of comparison of the methods of treatment, a five-year survival period has been selected. Included in this are certain patients who are known to have been suffering from recurrences or that developed these at a later date.

Table VI shows the total five-year salvage and is based on the number of patients seen.

TABLE VI. FIVE-YEAR SALVAGE OF TREATED AND UNTREATED PATIENTS

CONDITION 5 YEARS AFTER TREATMENT	PATIENTS	
	NUMBER	PER CENT
Alive	94	44.5
Dead	117	55.5
Total	211	100.0

FIVE-YEAR SALVAGE BASED ON METHOD OF TREATMENT

1. *Hysterectomy.*—In our clinic the operation of choice has been radical pan-hysterectomy, with removal of both adnexa when this procedure is not contraindicated.

From Table VII it will be observed that 115 patients were treated by hysterectomy. In this group are included those patients in whom irradiation was either preoperatively or postoperatively combined with hysterectomy, since we feel that in the

time covered by this analysis irradiation as an adjunct to surgery was not a routine measure and that the group is too small from which to draw any positive conclusions. Moreover, it is likely that the irradiation was in most cases inadequate. Of the 115 patients treated by hysterectomy, 55 patients survived five years or longer, a salvage of 47.8 per cent. Panhysterectomy was performed in 80 cases and supravaginal hysterectomy in 35. The reason for incomplete operation was in most cases either inability to remove the cervix, due to fixation by the malignant process, or a failure to suspect the condition in cases in which the diagnosis was made by histologic examination. When we compare the salvage in the two types of hysterectomies, we see that the salvage favors the complete operation, the proportion being 53.7 per cent as compared to 34.3 per cent. In the years prior to the use of irradiation no further treatment could be instituted, whereas today radium can be applied to the cervical stump and roentgen ray therapy be employed, thus yielding a more favorable prognosis in those cases in which complete hysterectomy cannot be performed.

2. *Irradiation.*—Eighty-nine patients were treated by means of curettage and irradiation. Thirty-nine patients, 43.8 per cent, survived the five-year period. Although definite changes as regards the total dosage in the initial irradiation of fundal carcinoma have taken place in the last five years, the average dosage in this series was only 2,400 mg. hours. Today this amount of irradiation is considered

TABLE VII. FIVE-YEAR SALVAGE BY METHOD OF TREATMENT

TREATMENT	PATIENTS		
	NUMBER	ALIVE	PER CENT
Hysterectomy	115	55	47.8
Radium	89	39	43.8
Untreated	7	0	0
Total	211	94	44.5

inadequate, but even with this small dosage, it was still of distinct curative value in over 40 per cent of cases, nearly all of which were poor operative risks. This does not take into consideration prolongation of life in hopeless cases and the greater comfort which accrues. In comparing our results as to methods of treatment, the salvage is approximately the same in the group treated by hysterectomy as in those treated by irradiation alone, namely, 47.8 per cent and 43.8 per cent, respectively. In comparing the two methods of treatment it should be remembered that of the patients treated by hysterectomy, only 74.8 per cent were traced, whereas of those patients treated by irradiation, in general a more recent group, 92.1 per cent were traced. In comparing the salvage in the patients treated by *panhysterectomy,* whether alone, preceded by, or followed by irradiation to the salvage in the patients treated by radium alone, the salvage favors complete hysterectomy in the proportion of 53.7 per cent to 43.8 per cent. Although our figures as regards salvage do not vary unduly in the two methods of treatment, the procedure of choice is considered to be radical panhysterectomy in the operable cases, followed by deep roentgen ray therapy. In the advanced or inoperable cases of fundal carcinoma, or in those in whom some contraindication to a radical operation exists, irradiation is the method of choice. From our statistics, no conclusions as to the rôle of radium as a preliminary treatment to hysterectomy can be reached, because of the small dosage that has been employed.

Tables VIII, IX, and X show five-year salvage in five-year periods with the exception of the years 1900 to 1910 in the patients treated by hysterectomy, radium, and the combined five-year salvage on all patients who were treated.

TABLE VIII. FIVE-YEAR SALVAGE IN CASES TREATED BY HYSTERECTOMY

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	15	20.0	60.0
1911-1915	19	36.8	68.4
1916-1920	25	52.0	80.0
1921-1925	37	59.4	78.4
1926-1930	19	52.6	78.9
Total	115	47.8	74.8

TABLE IX. FIVE-YEAR SALVAGE IN CASES TREATED BY RADIUM

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	0	0.0	0.0
1911-1915	1	0.0	100.0
1916-1920	18	44.4	88.8
1921-1925	30	36.6	90.0
1926-1930	40	50.0	95.0
Total	89	43.8	92.1

TABLE X. COMBINED FIVE-YEAR SALVAGE ON ALL PATIENTS TREATED

YEAR	PATIENTS		
	NUMBER	SALVAGE PER CENT	FOLLOWED PER CENT
1900-1910	15	20.0	60.0
1911-1915	20	35.0	70.0
1916-1920	43	48.8	83.7
1921-1925	67	49.3	83.6
1926-1930	59	50.8	89.8
Total	204	46.1	82.3

CONCLUSIONS

1. Childbearing plays no part in the predisposition to fundal carcinoma

2. The chief symptoms are bleeding and discharge. Metrorrhagia was the first symptom noted in 80.5 per cent of the cases.

3. The average duration of symptoms was 17.9 months. If myomas and fundal carcinoma were associated, the average duration of symptoms was 21.8 months.

4. Only 43.8 per cent of patients sought treatment prior to one year after the onset of symptoms.

5. The preoperative diagnosis was positive in 67.9 per cent of cases, suspected in 16.6 per cent, and unsuspected in 15.5 per cent.

6. All uteri removed for what are believed to be benign lesions should be opened and the endometrial cavity inspected before the operation is completed.

7. Diagnostic curettage is the most certain method of detecting the presence of early fundal carcinoma and may be relied upon in practically all cases.

8. The association of myomas and fundal carcinoma occurred in 34.9 per cent of our cases.

9. Of 13 patients with involvement of the ovary treated five or more years ago, 6 survived the five-year period, and in 14 cases in which the parametrium was invaded, 3 survived the five-year period.

10. For uncomplicated cases, a radical panhysterectomy and bilateral salpingo-oophorectomy, followed by deep roentgen therapy, is the treatment of choice.

11. When curettage is performed in a suspected case, a minimum of 1,200 mg. hours of radium irradiation should be employed. If broken-up particles of carcinoma are left behind in the uterus, the irradiation tends to prevent dissemination, and if the case proves to be benign, bleeding is checked.

12. The five-year salvage in patients treated by hysterectomy was 47.8 per cent.

13. The five-year salvage in patients treated by radium alone was 43.8 per cent.

14. The operative mortality for the series was 3.4 per cent.

15. In the patients treated by hysterectomy, the operative mortality was 4.3 per cent, and in patients treated by radium, it was 2.2 per cent.

16. The absolute five-year salvage in the entire series was 44.5 per cent, and the relative five-year salvage was 46.1 per cent.

A CRITICAL STUDY OF THE LOW CERVICAL AND CLASSICAL CESAREAN SECTION OPERATIONS*

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THERE has been considerable controversy concerning the relative merits of the classical and the low cervical operations for cesarean section. Such a reaction is inevitable when a different technic is proposed for a procedure in which the standard operation is giving reasonably good results in the hands of well-trained surgeons.

The difference of opinion seems to arise from the fact that certain operators desirous of finding some way to minimize the inherent risk in cesarean section have adopted the newer operation and use it exclusively. Others, more conservative, either refuse to try the new procedure on the ground that it does not appeal to them as an improvement over the older operation, or else having tried it in a few cases, decide that it is not the operation of choice because of some technical difficulty which they may have encountered.

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*Read before the Chicago Gynecological Society, March 20, 1936.

The diversity of opinion may be appreciated by the expression of several outstanding authorities.

Williams[1] felt that the classical operation was preferable in those cases in which the probability of intercurrent infection was slight; where this probability was great he preferred the low cervical operation. Where evidence of infection could be demonstrated clinically he preferred the Poro operation.

Bland[2] advocates the classical operation in all patients who can safely be placed in the category called "clean." The low cervical operation is advised in those who have been long in labor with membranes ruptured or have had vaginal examinations, or other manipulation.

DeLee,[3] on the other hand, strongly favors the low cervical cesarean section. He claims that there is less hemorrhage, less ileus, less gastric dilatation and peritonitis, and that wound healing is better because the lower uterine segment following operation is at rest. He also claims that the maternal mortality of the low cervical operation is less than following the classical. These advantages would be quite significant if demonstrable. No proof is educed however to support this contention.

Beck[4] also favors the low cervical cesarean operation, claiming less danger because of limitation of the spill, the low position of the uterine wound tending to localize the infection in the pelvis in those cases in which infection develops. Less hemorrhage and distention and fewer adhesions. Again, however, these advantages are based on clinical impression, no proof is presented to support the contention.

I wish to point out several factors which may contribute to a false impression in evaluating the results obtained by the new operation.

The sponsors of the new procedure quote the results obtained in a given number of cases since its adoption. The apparent improvement in their results is attributed by them to the new procedure. No weight is given to the fact that they, after doing a considerable number of operations, using the old classical technic, are better prepared by that experience to do the next series of cases, no matter which technic is used.

As an operator grows in experience, so also there appears in his clinic a cooperation, attention to detail, and smoothness of execution by the resident and nursing staff and the anesthetists, all of which are important contributing factors in lessening the operative shock and reducing the operating time, which in turn inevitably reflects itself in improved operative results.

In some instances because of relative unfamiliarity with the new procedure, the old or classical technic is elected for the difficult cases. The low cervical operation is used only in those cases in which no technical difficulty is anticipated.

Not infrequently statistics from clinics are compared where the circumstances surrounding the operation are widely different.

Statistics of the present are unfairly compared with the statistics compiled years ago.

Results of trained obstetric surgeons are contrasted with those of general practitioners in a given community.

The conservative, on the other hand, will have nothing to do with the new procedure because the principles involved do not appeal to him. Or

he will give it up after a trial or two because of some difficulty encountered, or poor results. He has obtained good results, with the older procedure, low mortality and morbidity, and cannot see the advisability of changing to the new technic until its advantages are conclusively demonstrated.

How then are we to arrive at a reasonable estimation of the value of a new procedure, since we have to rely almost entirely on the published reports of men who have a more or less biased viewpoint, and whose published results cannot but reflect the same.

One rational method of settling such disputes is extremely simple and satisfactory, even though somewhat slow. If an operator will set himself to the task of alternating the two operations on the cases as they present themselves for operation, the results will speak for themselves as soon as a sufficient number of cases have been accumulated. The personal equasion is thus reduced to the minimum.

Certain advantages are claimed by the sponsors of each operation.

The advocates of the low cervical operations claim for its superiority on the ground that:

1. Wound healing is better because the lower uterine segment is passive during the puerperium, and therefore better healing is promoted.

2. There is therefore less likely to be a rupture of the uterus in subsequent pregnancies.

3. Infection if it occurs and pentrates the uterine wound will be limited to the extraperitoneal space behind the bladder, for a time at least, before producing infection of the general peritoneal cavity.

4. The operation is usually completed without the intestines coming into view, reducing thereby the danger of peritoneal contamination and ileus.

5. There is less postoperative discomfort, vomiting, and ileus following the low cervical operation.

6. There is less danger of adhesions forming between the uterine and abdominal wound.

The advocates of the classical operation say:

1. That there is no evidence that the wound healing takes place under any more quiet conditions in the low cervical than in the classical operation.

2. That the thicker the surfaces of uterine muscle that are approximated the better the scar.

3. That there is less danger therefore of rupture of uterine scar in subsequent pregnancies.

4. That when properly done in noninfected cases, there is very little danger of infection coming through the uterine wound.

5. That the low cervical section is more dangerous, time-consuming, and technically more difficult.

6. That there is more danger from hemorrhage when the placenta is in the lower uterine segment.

7. That there is no reason for exposure of the bowel or more contamination of the peritoneal cavity in the classical operation.

8. That there is less danger of bladder injury and cystitis.

It was in the hope of throwing some light on these questions that this series of operations was undertaken.

I have, in the last ten years, collected a series of cesarean sections personally done in the same clinic, under identical conditions. As nearly as possible the cases were alternated. There was no deviation in favor of either operation because of potential infection, placenta previa, serious toxemia, or other complications. The results, therefore, although the series is not large, should speak definitely as far as they go for the relative merits of the two operations.

In order to place clearly before you how these patients were treated, I shall give a brief outline of the technic of both operations as done in my clinic.

In the classical operation the following steps were carried out:

1. The patient is placed in the Trendelenburg position after preparation of skin with iodine and alcohol as for ordinary laparotomy.

2. A midline incision is made from just above the pubes almost to the umbilicus.

3. The uterus is rotated if necessary to bring the midline of the uterus into the center of the abdominal wound.

4. An incision is made in the anterior uterine wall beginning just above the vesicovaginal peritoneal fold and extending upward about 12 cm.

5. The baby is delivered by grasping a foot and extracting by the breech.

6. Pituitrin 1 c.c. obstetric is injected into the uterus.

7. The edges of the uterine wound are grasped by Allison forceps on each side and the placenta and membranes are delivered manually.

8. Ergotol one ampule is given hypodermically as soon as the placenta is delivered.

9. The uterine wall is repaired, with the uterus in the abdomen as a rule, with four layers of chromic catgut as follows: The first row of sutures is a continuous double No. 2 chromic catgut suture, starting near the pubic end of the wound and taking about half the thickness of the uterine wall, extending down to but not through the mucosa of the uterus. When this stitch is tied at the upper end of the wound the uterine cavity is effectively closed off. The next stitch beginning at the lower end of the wound and continuing to the upper end is made by inserting the needle just under the serosa and carrying it down to interdigitate with the preceding row of stitches. The next layer approximates the edges of the serosa and interdigitates with the second layer. The final layer is the peritonealizing layer. It is done with fine catgut. The loose vesicouterine peritoneum on each side of the lower end of the wound is sewed over the wound from below upward. It will be found that in most cases about half of the wound can be covered by this loose peritoneum. From here to the upper end of the incision, the peritoneum and a small bit of the muscle on each side of the wound are caught in each stitch which when drawn tight buries the scar. The free blood and clots are removed from the abdominal cavity, and the abdominal wound is closed in layers.

The technic for the low cervical operation was as follows:

1. Position, preparation, and abdominal wall incision are the same as in the classical operation.

2. The loose peritoneum between bladder and lower uterine segment is raised and cut transversely from one broad ligament to the other. The lower leaf is pushed down with the bladder off the lower uterine segment.

3. The latter is incised in the midline, care being taken to avoid cutting the baby, since the lower uterine segment is very thin. The fetal head is then rotated so that the occiput points into the wound, forceps are applied and the baby is gently extracted.

4. **Pituitrin** and ergot are given as before and the placenta is either expressed or delivered manually.

5. **The edges** of the incision are about 2 mm. thick, except at the upper angle of the wound where invariably the upper uterine segment is invaded in all cases that have not been in labor. The edges are grasped by Allison forceps and closed by a running No. 2 chromic catgut suture. Often a second continuous stitch can be placed in the uterine muscle. Next a thin layer of fascia between the bladder and uterus is closed over the uterine wound. The transverse incision in the peritoneum is sewed over the wound with No. 1 plain catgut. In case infection is strongly suspected, I push the bladder off the anterior vaginal wall, incise the latter and put a drain into the vagina. The upper part of the drain lies on the scar in the uterine wall. Any seepage from the uterine cavity is thus led directly into the vagina. The drain is removed in forty-eight hours if no infection occurs. The peritoneal cavity is then freed of blood and clots and the abdomen closed in layers.

In estimating the results in the two series of cases several factors were thought to be of importance to determine the comparative morbidity, reaction, and distress. The age and parity were noted because obviously a great difference either way in either group might have a significant bearing. The indication for operation was also noted because a patient with placenta previa or severe toxemia might be a poorer operative risk than one with a contracted pelvis. For the same reason the cases complicated by syphilis were also noted as well as all those having evidence of associated nephritic or preeclamptic toxemia.

The operating time was observed for two reasons: because of the bearing that this might have on shock, hemorrhage, and infection, and to determine to some extent thereby the relative technical difficulty of the two operations. For the same reasons the type of anesthesia was recorded. Vomiting and partial ileus were taken as a rough measure of the peritoneal reaction following the invasion of the peritoneal cavity. The number of times vomiting occurred postoperatively and the number of enemas necessary to produce flatus and relieve distention were taken as the measure of the ileus.

The highest temperature on the days in which the temperature reached 100° or more postoperatively was recorded and supplemented by the report of wound infection and the number of days the patient remained in the hospital after operation was taken as the index of morbidity.

The amount of postoperative discomfort and pain was roughly measured by the amount of morphine administered postoperatively. Our routine for postoperative treatment is a quarter of a grain of morphine if there is discomfort a few hours after operation and a sixth of a grain every four hours as necessary subsequently.

In addition, we noted the number of catheterizations necessary postoperatively because of the general impression that the low cervical operation is more likely to give rise to bladder irritation and complications.

We also noted whether or not the membranes were intact or ruptured before operation, because of the obvious bearing on potential infection.

The weight and length of the baby were also recorded together with the condition at birth and the final outcome.

The results obtained from the study of these cases are interesting for several reasons. The average age was found to be 24 in the low cervical and 25.7 in the classical group; there were 37 multiparas and 20 primiparas in the low cervical cesarean section group, and 35 multiparas and 22 primiparas in the classical group.

The indications for operation are seen in Table I. It will be noted that there was no great preponderance of pathologic cases in either group.

TABLE I. CLINICAL CASES

		57 CASES LOW CERVICAL	57 CASES CLASSICAL
Indications:	Placenta previa	10	3
	Premature detachment	8	11
	Heart lesions	3	6
	Contracted pelvis	15	17
	Eclamptogenic toxemia	8	6
	Miscellaneous	7	3
	Previous cesarean	12	15
Age:		24	25.7
Para:	Primipara	20	22
	Multipara	37	35
Wassermann:		5	2
Toxemias:	Preeclamptic	12	11
	Thyroid	0	2
Operating Time:		43 min.	44.4 min.
	Sterilizations	13	16
Anesthesia:	General	53	46
	Local	4	11

TABLE II. CLINICAL CASES

	57 CASES LOW CERVICAL	57 CASES CLASSICAL
Vomiting total number	19	28
Ileus partial	4	8
Temperature above 100°		
Average days per case	3	4.37
Days in hospital		
Average postoperative	15	16.4
Average amount of morphine		
Postoperatively per case	$6/12$ gr.	$7/12$ gr.
Total number of catheterizations	16	33

The average operating time was forty-three minutes in the low cervical series and forty-four and four-tenths minutes in the classical series. This result may have been influenced by the fact that 11 of the classical cases were done under local anesthesia, which always slows up the operation, to 4 of the low cervical, and, also, to the fact that one of the classical cases had a ventral hernia which was repaired after sewing up the uterus. Other factors which would add to the operating time such as

sterilization by exsection of the uterine end of the tube and adhesions due to previous cesarean sections were about equal in the two series.

I was somewhat surprised by the result since the commonly accepted view is that the low cervical operation is technically more difficult and more time-consuming. From my experience I should say that the operation is not appreciably more difficult and that there is practically no difference in the operating time if the conditions for the operation are the same.

The anesthesia most used in both series was ethylene, to which was added a small amount of ether, just as the abdomen was opened to secure better relaxation. In the classical group 11 had local anesthesia, 1 per cent novocaine with no preliminary morphine and scopolamine, because of the danger of depressing the respiratory center of the baby. Only 4 of the low cervical group were done under local anesthesia. There was no special reason for the discrepancy in this respect in the two groups since technically the operation under local anesthesia is not difficult. A small number of each series had ether only and a few had nitrous oxide only.

As an indication of the postoperative shock, ileus and peritoneal reaction, we observed the number of times the patients in each series vomited postoperatively, and, also, the cases that had to have repeated enemas to relieve the gaseous distention postoperatively.

In the classical group, emesis occurred 28 times, while in the low cervical group it occurred 19 times. In the classical group, 8 cases had sufficient obstipation to be classified as mild ileus, while 4 of the low cervical cases were so classified.

In the classical group the average postoperative days in which the temperature reached 100 or more was 4.37. In the low cervical group the number of temperature days was 3.

The number of postoperative hospital days for the classical group was 16.4 as opposed to 15 for the low cervical group.

Wound infection occurred in 4 of the classical cases while only 2 of the low cervical cases had wound infection.

As an index of the postoperative discomfort, it is interesting to see that the average amount of morphine given in the classical cases was $7/12$ of a grain, while the average for the low cervical cases was $6/12$ of a grain. The difference is hardly appreciable.

The membranes were ruptured for a short time before operation in 4 patients in the classical series, while in the low cervical series the membranes had ruptured in 3 patients.

As a rough measure of functional bladder disturbance following the two operations, the number of postoperative catheterizations was taken. It was found that catheterization was necessary 33 times in the classical

series, and only 16 times in the low cervical group. The often quoted danger of bladder traumatization in the low cervical operation seems to be theoretical rather than real according to these figures.

There was one death in this series which occurred in the classical group. A brief description of the case is as follows:

A para x, twenty-six weeks pregnant, entered the hospital with a diagnosis of severe nephritic toxemia. Because of the prematurity of the baby, an attempt was made to carry the patient along until viability. This was carried out for twenty-six days in spite of severe symptoms which did not yield in medical management. Finally when the baby seemed to be on the borderline of viability, we did a cesarean section under local anesthesia. This was accomplished without difficulty in forty-seven minutes, including sterilization. The patient developed a peritonitis and bronchitis and died on the fourth day. The anatomic diagnosis at the postmortem examination was as follows:

Generalized peritonitis, extreme fatty degeneration of the liver, early arteriosclerosis and arteriolosclerosis of the kidneys with marked fatty degeneration, early bronchopneumonia of the right upper lobe, marked congestion of both lungs, hypertrophy of the thyroid, and puerperal uterus with recent ulcerative colitis.

I do not feel that the disastrous outcome in this case can be attributed solely to the operative procedure. I should rather attribute it to faulty judgment on my part in trying to prolong gestation to viability of the baby in the face of a toxemia not responding to medical management. The decision to do a cesarean section instead of induction of labor was based on the fact that the fetal heart tones suddenly became very irregular, varying from 80 to 160 beats per minute. The uterus at postmortem was a normal puerperal uterus so that the peritonitis was not due to faulty healing of the uterine wound.

In addition to the above described series of cases done in my clinic, I have operated upon 49 patients at various private hospitals in Chicago. Twenty-three classical and 26 low cervical operations were done. The preoperative and operative factors are shown in Table III and the results are shown in Table IV.

In this series the results are practically the same as in the previous series. Age, parity, and anesthesia were practically the same for each group. The patients in the low cervical series were in the hospital one day less but ran a slightly higher temperature, and showed much more vomiting, slightly less ileus and less bladder irritability. There was slightly more pain since ⅙ gr. more of morphine was used in these cases. The operating time was about equal which is the more significant since assistants were different in most of the cases. There was no mortality in either group. The total morbidity in this series seems to be slightly less in the classical group.

It would seem therefore that the same conclusions, namely, that if done by the same operator there is no appreciable difference in the results obtained by the two operations, whether done on clinical patients with the same type of assistance in the same hospital or whether done in different institutions, with different assistants on private patients.

TABLE III. PRIVATE CASES

		26 CASES LOW CERVICAL	23 CASES CLASSICAL
Indications:	Placenta previa	1	0
	Premature detachment	2	1
	Heart lesions	0	0
	Contracted pelvis	9	3
	Eclamptogenic toxemia	7	7
	Miscellaneous	2	9
	Previous cesarean sections	3	3
Age:		29.8	30.9
Para:	Primipara	15	10
	Multipara	11	13
Wassermann:		0	0
Toxemias:	Preeclamptic	7	7
Operating Time:		43.6	43
	Sterilizations	1	0
Anesthesia:	General	23	21
	Local	3	2

TABLE IV. PRIVATE CASES

	26 CASES LOW CERVICAL	23 CASES CLASSICAL
Vomiting total number	15	5
Ileus partial	9	11
Temperature above 100°		
Average days per case	3.2	3
Days in hospital		
Average postoperative	14.2	15.4
Average amount of morphine		
Postoperatively per case	$\frac{6}{12}$ gr.	$\frac{8}{12}$
Total number of catheterizations	16	21

From the foregoing it will be seen that there is no significant difference in the results obtained in the two series. The clinical group showed slightly more morbidity in the classical series. The private group showed a little more morbidity in the low cervical series. In both groups the bladder irritability was less marked in the low cervical and was insignificant in both groups. An indwelling catheter was not used in any of these cases. None of them was complicated by postoperative pyelitis or serious cystitis. Since in the larger group of clinical cases there was a slight apparent increase in morbidity, the burden of proof seems to lie with those who claim the classical operation is the operation of choice. Since, however, the difference between the results is so small in my hands, I feel justified in continuing the experiment I have started until I have accumulated more evidence. It would be desirable for other clinics interested in the subject to adopt this method so that comparable statistics might be compiled.

CONCLUSIONS

1. As regards morbidity and mortality in the series, there appears to be a slight difference in favor of the low cervical operation.

2. As regards postoperative vomiting, ileus and temperature days, hospital days and wound infection, there appears also to be a corresponding slight difference.

3. There seems to be no difference in the postoperative discomfort.

4. There seemed to be less bladder dysfunction after the low cervical than after the classical operation.

5. There is no appreciable difference in the technical difficulty as measured by the operating time.

6. The results obtained by the low cervical operation are hardly so superior to those following the classical operation as to justify the extravagant praise of some of its sponsors.

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30 NORTH MICHIGAN BOULEVARD

DISCUSSION

DR. WILLIAM C. DANFORTH.—For many years we did the classical operation as a routine procedure, reserving the low cervical for women who had gone into labor, or whose membranes had ruptured, or when a test of labor had been decided upon. Our impression is the same as Dr. Falls', but we feel the superiority of the low cervical operation is more marked. I do not know whether he alluded to the management of relative contraction in which a test of labor is used. It seems to me that in those cases particularly, the superiority of the newer technic is quite definite. It has been so in our experience. Formerly when we did classical section upon a woman in labor or one whose membranes had ruptured, the convalescence was very definitely stormy. Our convalescences in low cervical sections have been quite definitely better. Since 1922, through 1935 and not counting the cases in 1936, we have done 341 low cervical sections. In the same period the classical section was done only 60 times. Some years ago I looked up our mortality with classical section, and it was 4 per cent. I think the large mortality was due in part to the toxemia or eclampsia from which the women suffered, because when I first went into practice we were delivering all patients with eclampsia by one or the other operative means. The mortality for the patients who had 341 sections since 1922 is 0.87 per cent. In almost 50 per cent a test of labor had been carried out. It seems to me that the low cervical operation is definitely superior to the classical not only from the standpoint of mortality, but also from the standpoint of morbidity, as recoveries have been smoother with the new type of operation than with the older.

As to the low cervical section in placenta previa, we formerly preferred the classical. In late years we have done the low cervical on almost all patients with placenta previa. I think in some cases of central placenta previa the older operation is still preferable, but the risk of the new operation in placenta previa is no greater than in the old. Bleeding sinuses may be stitched over if needed, and one can pack more easily than with the classical. I agree with Dr. Falls except that we believe the superiority of the new operation is greater than his experience has shown.

DR. RUDOLPH W. HOLMES.—My cesarean experience covers a period of over thirty-six years; during that time I have seen the furor aroused by the advocates of one variant in technic to another: in this period the sites for the diverse uterine incisions, if made continuous, would sagittally bisect the uterus from the cervix anteriorly to the same structure posteriorly: and numerous coronal incisions have been recommended. I have never been swayed by the enthusiasms of proponents for one or the other. Three factors influence cesarean section mortality: the first, and most fundamentally important element, is the indication. The range covers the operation for eclampsia where the fatality is the highest, and is lowest, occurs in contracted pelves, where the patient is otherwise perfectly well, or where the unjustifiable operation is performed as a "matter of convenience."

The second factor is the environment in which the operation is done: hospitals which have perfectness of cooperation of the personnel, and operating room equipment complete in every detail, will have a relatively low mortality, whereas, where the converse holds true the mortality rate necessarily will be high.

The third factor is the operator: he who carefully "selects" patients who will be safe surgical risks will have a low mortality—but, if patients are selected for operation, and then the operation is rejected on account of extraneous circumstances, and ultimately have a spontaneous termination of labor, it is prima facie evidence that the primary placing of the indication for cesarean was spurious. The man who meticulously carefully adheres to the tenets of conservative obstetric principles and operates on pressing indications will necessarily have a considerable mortality.

In 1922 I reported 92 cesarean sections before the American Gynecological Society, among which were 6 maternal deaths (2 were eclamptic patients with pelvic contraction which dictated the operation) and 8 fetal deaths, of which 2 were still born; 2 were hydrocephalic, the operation being indicated for gross pelvic deformity; and 4 died within fifteen days from nonobstetric causes.

After reading the paper, one of the outstanding proponents of the low cervical cesarean section, which then was newly revived, told me I would not have had the high thermal reactions if I had performed the low cervical operations—an operation practically unknown during the period in which most of my operations were performed!

In my paper the operations were grouped into those patients not in labor, those in labor, and those with membranes ruptured; the high and low temperatures for ten days were recorded; the averages for each group were recorded and charted. The exponent of the new cervical section had recently reported his series with the temperature charts. I took his 7 operations which had been longest in labor with membranes ruptured, and the same number of mine. In his series the duration of ruptured membranes ranged from thirty-six to seventy-two hours, an average being fifty-one hours while mine ranged from twenty-four to eighty-four hours, average fifty-two hours: the average duration of labor in his patients was forty hours, while mine was forty-six hours. The high and low temperatures of the several groups were averaged for the ten days, and a chart made which I show you. You will note that operative results, as far as the temperature is concerned, do not compare with mine. You must remember that my series covers the period from the time when an Esmarch constriction about the cervix was deemed essential, and the period when eventration of the uterus was considered the wise expedient. But temperature alone is not the sole criterion: Dr. Falls has presented indisputable evidence that the type of operation is relatively immaterial and irrelevant—success is more determined by the given operator and his environment than any and all other influences. Enthusiasm for a new operation dims an operator's perspective—and his deductions are prone to be fallacious; too, a comparison of results of recent cervical sections with past experiences with classics is grossly faulty.

I have in preparation a survey of cesarean section in 420 American hospitals. It is too early to offer much advanced information, but I would cite a few facts.

In one hospital there were 22 classic operations with a mortality of 4.5 per cent, while in 7 cervicals the mortality was 14 per cent. In another hospital 12 classics had no mortality, while in 15 cervicals the rate was 6.6 per cent. In still another hospital the classic rate was 4.9 against 9 per cent for cervical. One hospital had 72 classics and 70 cervicals without maternal mortality.

Dr. Falls has definitely proved his contention that the place of the incision is inconsequential; the crux of the situation lies in the operator himself.

DR. RALPH A. REIS.—I should like to ask Dr. Falls if he now advocates a low cervical cesarean in contradistinction to the classical type? Also, has he found that one of the advantages of the low cervical type is the lack of postoperative adhesions involving the omentum, uterus, and bowel? We have found at Michael Reese Hospital that when we do low cervical section, we have had less adhesions than following the classical type of operation. Dr. Falls in his series had a large number of repeat cesarean sections, and I wonder if he could clear up that point. It would seem that with the bladder covering the lower segment there should be less adhesions following the low cervical operation, and I should like to know whether Dr. Falls' experience has been the same as ours.

DR. FALLS (closing).—Dr. Danforth's point about doing the low cervical operation after the test of labor is well taken. As a result of this study I believe in such cases the low cervical operation is indicated. In our series, however, no deviation in favor of the low cervical operation was practiced in such cases. One should be careful in interpretation of clinical impressions as mentioned by Dr. Danforth. The actual figures gathered in this study upset several of my previous impressions.

The cesarean section as practiced in this series for eclampsia and eclamptogenic toxemia resulted in one death in 28 cases, a mortality of 3.5 per cent.

In placenta previa, I do not think it makes any difference whether one does a low cervical or a classical operation. There is a possible advantage to being able to see a bleeding point while doing a low cervical, but we have never sutured a bleeding point in a low cervical, though we have done more of these operations than classicals in placenta previa. After taking out the placenta, if there is bleeding, we pack the lower uterine segment and sew over the pack. Theoretically and practically there is no question but that one could put in a stitch. It is rarely necessary.

The point stressed by Dr. Holmes that the individual operator may change the result in comparing these operations, is very important. That is why I did every operation myself from start to finish. All fever we ascribed to inflammation and not to thermal reaction, which as Dr. Holmes said is "quibbling." As far as postoperative adhesions are concerned, we have opened the abdomen subsequently in several patients and we did not see very many adhesions with the classical operation, done as we do it. I think postoperative adhesions come from one thing, that is peritonitis. Evidence that there is less peritonitis in the low cervical operation than in the classical operation is lacking in this series.

Harrisson, E. H.: **The Eynesbury Quadruplets**, Brit. M. J. 2: 1207, 1935.

An account of the delivery of these quadruplets is given. Nothing is unusual in the management of the case. The placenta is of interest. It appears that three ova were fertilized, and the first two infants were bi-amniotic twins from one ovum. It appears then that one, two, three, or four ova may be involved in the production of quadruple pregnancy.

F. L. ADAIR AND S. A. PEARL.

ANALYTICAL STUDY OF 347 CONSECUTIVE CESAREAN SECTIONS

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CESAREAN section is accompanied by a greater morbidity and mortality than uncomplicated simple laparotomy. It would appear from a study of the situation that the technical surgery involved is far less important than a well-organized effort to intelligently interpret and evaluate the attendant general and obstetric status of the patient. Mature deliberate obstetric judgment plays a much more important rôle than the equally necessary obstetric operation. Improvements in technic and a more comprehensive understanding of the conditions under which the abdominal route may be preferred have substantially reduced the initial risk. In weighing the hazards of fetal injury or extensive maternal damage, suprapubic delivery is often chosen as a solution of the problem.

INDICATIONS FOR OPERATION

We have adopted the classification of indications as outlined by Gordon,[1] with such modifications as are explained under the proper headings. The plan of grouping has been:

1. Cases of contracted pelvis.
2. Cases of eclampsia and other toxemias of pregnancy.
3. Cases of antepartum hemorrhage (placenta previa and accidental hemorrhage).
4. Other conditions.

The most frequent indication for section was contracted pelvis, totaling 206 cases or 59.3 per cent. In the second group were 7 cases of eclampsia and 14 cases of preeclampsia. The third group was composed of 23 cases of placenta previa and 9 cases of ablatio placentae, 4 total and 5 partial. Among other conditions were listed the following:

Cardiac disease	14
Disproportion	24
Cervical dystocia	19
Multiple fibroids	5
Breech	2
Persistent occipitoposterior	3
Habitual stillbirth	2

and 1 each of the following:

Interposed uterus

Ruptured uterus

Paraplegia following encephalitis

Previous third degree laceration

Torsion of uterus

Ventral fixation

Hemiplegia

Transverse presentation

Psychosis

Previous myomectomy

Previous poliomyelitis

Hypertension

Hemiplegia plus hypertension

Pulmonary tuberculosis with unengaged
    head

Kyphotic pelvis in an elderly primipara

Three hundred and forty-seven cesarean sections were done by 20 surgeons, representing 1.56 per cent of 23,031 total deliveries during a thirteen-year period up to December, 1935. Of these, 163 were of the classical type. Our feeling has been that there is still a definite field for the classical operation and where the results have been bad, investigation has usually revealed the use of faulty judgment in the selection of the case; 126 were of the low two-flap Beck operation; 47 were of the low transverse cervical operation popularized by Phaneuf. There were 6 classical cesarean sections with extraperitonealization of the uterine incision; there were 3 cesarean sections with hysterectomies of which two were done for fibroids plus pregnancy and the third for a neglected case following a previous interposition operation. During the past year the low transverse cesarean section has been adopted by some members of the staff, and my conclusion is in agreement with the claims of Phaneuf.[2] It had been noted that when the low cervical longitudinal uterine incision was employed it was sometimes found necessary to extend it superiorly into the body of the uterus when delivering a large fetal head. This resulted in a failure to secure all the advantages that accrue in keeping the uterine incision below the isthmus. Also, when the operation was performed before term, the lower segment was found to be too short to permit the easy access of the fetus. Finally, less separation of the bladder from the cervix was found necessary.

The classic cesarean section with extraperitonealization of the uterine incision, in which the parietal peritoneum is sutured around the uterine incision, was done in 6 cases by one member of the staff with uniformly bad results. High morbidity, marked abdominal distention, considerable vomiting and scant foul lochia were predominant. There appeared to be a restraining interference with the normal contraction and retraction of the uterus with resulting delayed involution of the latter.

1. *The contracted pelvis group* included 55 cases of absolute contraction in which the indication was obvious and the delivery by cesarean section, either elective or following a short trial labor. The larger proportion were border-line contractions which necessitated the most deliberate obstetric judgment in their management. Many of these patients had entered the hospital with membranes ruptured; in others the membranes ruptured soon after admission. Most of these women developed poor ineffectual pains, usually accompanied by a maladjustment of the presenting part, and a discouragingly slow cervical dilatation. The crucial decision has been to determine where the margin of safety ends beyond which is the specter of an exhausted mother with diminished resistance to hemorrhage and infection, and a badly jeopardized baby. The recent epochal work of Caldwell and Moloy[3] and Thoms[4] in cephalopelvic relationship gives promise of more precise appraisal of cases of disproportion without recourse to a dangerously long trial test of labor. This group includes those with a previous obstetric history of prolonged labor and difficult instrument delivery, resulting in forbidding maternal and fetal damage. There were 41 resectioned cases, of which 39 were done for cephalopelvic disproportion; one for paraplegia, and one for recurrent placenta previa. Thirteen of this group were sterilized.

2. *In the preeclampsia series* (second group), the abdominal route has been referred for those severe preeclamptic patients who fail to respond to intensive well-directed therapy and become progressively worse. In cases where convulsions have already occurred, we have followed the accepted teaching that cesarean section is contraindicated and belongs in the same category with accouchement forcé. The occasional exception has been prompted by the feeling that "cesarean operation has a distinct though limited place and in cases where delivery by vaginal route offers great difficulty and where no improvement in the toxic condition is observed, after a reasonable application of sedative and eliminative measures, cesarean section with local anesthesia offers the best hope for a successful outcome" (Schulman).[5]

Third Group.—In both the primipara and multipara near term with moderate or profuse bleeding and with an undilated cervix, our present preference is delivery by cesarean section irrespective of the type of placenta previa.

Ablatio Placentae.—Cesarean section has been resorted to only in selected cases presenting signs of acute hemorrhage, either of the concealed or the frank variety, with an undilated cervix. In both of the foregoing groups, transfusion before operation has been a routine measure.

Fourth Group.—We have felt that most cardiac patients can be delivered safely from below. Nature often appears very kind to those so afflicted, and the ease of their delivery very often furnishes an agreeable surprise. In selected instances most of which have been cases of mitral stenosis, occurring in primiparas with a previous history of decompensation, the condition has been considered sufficiently serious to warrant abdominal delivery. This has applied particularly to those patients whose cardiac condition would be unlikely to tolerate safely the second stage expulsive efforts. This includes both the immediate risk as well as permanent residual additional pathology to an already damaged heart. The majority of these patients were sterilized, the former being a contributing indication for operation.

Interposed Uterus.—This rather unusual case is reported in detail. Case of multipara, forty-one years of age, full term, with history of previous uterine interposition done at another institution two years before, without sterilization. Admitted after three days of active labor at home under care of midwife; membranes ruptured four days; innumerable vaginal examinations. Temperature on admission 102°, pulse 140, spastic uterus, marked thyrotoxicosis; cervical stump barely admitting finger tip. Cesarean section and hysterectomy, recovery.

TYPE OF ANESTHESIA

One hundred and ninety-five patients had spinal anesthesia alone with one anesthesia death, which occurred before operation was begun; 123 patients were given ether and 8 cases induction gas followed by ether; 20 were done under local infiltration and 1 under sacral anesthesia.

Coincidental operations included 15 sterilizations and 1 myomectomy.

CONDITIONS AFFECTING MORBIDITY AND MORTALITY

A study of Table I reveals an increase in the morbidity rate in direct proportion to the time interval between the operation and the onset of labor plus ruptured membranes as shown so well in the survey of C. A. Gordon. The safe interval appears to be six hours after rupture of membranes or after the onset of labor. Following this there is an uncontrollable steady rise in the morbidity rate. It is likewise

apparent that the preoperative vaginal examinations must be reduced
to the minimum if satisfactory morbidity standards are to be obtained.
The standard taken for morbidity was a rise in temperature of 100.4°
on any two successive days after the first day.   Table II shows the
causes when determined.

TABLE I.   CONDITION AFFECTING MORBIDITY AND MORTALITY[6]

1. *Membranes ruptured*

HOURS	TOTAL	MORBID	PER CENT	FATAL	PER CENT
0-12	259	50	19.1	10	3.8
12-24	40	11	27.5	2	5.2
24-48	22	9	40.9	2	9.09
48 or more	9	5	55.5	2	22.2
Not determined	17	5	29.4		

2. *Vaginal examinations*

NUMBER OF EXAMINATIONS	TOTAL CASES	MORBID	MORBIDITY PER CENT	FATAL
One	43	15	34.8	1
Two	4	2	50.0	2
Three	4	2	50.0	0

3. *Hours in labor*

HOURS	CASES	MORBID	MORBIDITY PER CENT	FATAL
0-12	173	19	10.9	10
12-24	67	21	31.3	3
24-48	84	31	36.9	2
48 or over	23	9	39.1	1

TABLE II.   CAUSES OF MORBIDITY

Wound infection	19	Pyelonephritis	1
Lochia metra	19	Pneumonia	1
Thrombophlebitis (Saphenous)	2	Pulmonary infarct	1
Pyometra	1	Pelvic abscess	2
Parotitis	1	Pyelitis	4
Sapremia	14	Evisceration and pneumonia	1
Parametritis	6	Undetermined	8

Total number of cases with morbidity, 80 or 22.9 per cent.

CAUSES OF MATERNAL MORTALITY

There were 16 maternal deaths in this series of 347 cases, or 4.61 per cent.   The
causes were as follows:

Spinal anesthesia	1	Perforated peptic ulcer	1
Ruptured uterus	1	Pneumonia	3
Placenta previa	1	Pulmonary infarct	1
Peritonitis	4	Ablatio placentae	1
Sepsis streptococcemia	1	Nephritis uremia	1
Psychosis	1		

Of the foregoing, 3 cases, namely, the spontaneous rupture of the uterus, the
perforated peptic ulcer, and the psychosis, are due to extraneous causes.   Deducting
these three gives us a corrected mortality of 3.74 per cent.

FETAL MORTALITY

STILLBORN	16 OR 4.61%
1. Premature separation of the placenta	6
2. Porro performed with fetus in utero	1
3. Mother died of spinal anesthesia: fetus left in utero	1
4. Placenta previa	4
5. Atelectasis	2
6. Toxemia	1
7. Ruptured uterus	1

Of the aforementioned, all six babies in the premature separation group were dead before operation. Eliminating these together with the two babies left in utero and the ruptured uterus case gives a corrected mortality of 2.01 per cent.

NEONATAL

1. Hydrocephalus	1
2. Heart anomaly	1
3. Toxemia	2
4. Esophageal stricture	1
5. Cerebral hemorrhage	1
6. Prematurity	1
7. Placenta previa	1

In this group eliminating the hydrocephalus, heart anomaly, esophageal stricture, and prematurity, gives a corrected mortality of 1.15 per cent.

TABLE III.   MORTALITY AND MORBIDITY ACCORDING TO TYPE OF SECTION

METHOD	CASES	MATERNAL MORBIDITY	PER CENT	MATERNAL MORTALITY	PER CENT	FETAL MORTALITY	PER CENT
Classic	163	35	21.4	8	4.9	12	
Low cervical two-flap	126	34	26.9	7	5.5	3	2.4
Low cervical transverse	47	11	23.4	1	2.1	0	0.0
Classic with extra-peritonealization of the uterine incision	6	5	83.3	0	0.0	0	0.0

MORTALITY

Anesthesia.—Patient, aged thirty-two years, para i, admitted after thirteen hours in labor. Membranes intact; no engagement of head. Cervix three fingers dilated. Fetal heart was good. Cesarean section attempted under spinal anesthesia. As abdomen was opened, patient died, due to respiratory failure. Postmortem examination revealed no cause of death except that due to respiratory failure attributable to the spinal anesthesia.

Ruptured Uterus.—The patient was a forty-four-year-old para ix, who had a vertex presentation; she had had ten hours of moderate labor pains and was three fingers dilated. For no apparent reason she suddenly became pulseless and went into extreme shock. The abdomen was rigid. No pituitary extract had been given. An immediate laparotomy revealed a rupture of the uterus at the cervicovaginal junction extending into the broad ligament. She died on the operating table.

Placenta Previa.—Primipara, aged twenty-four years, full term, admitted with a history of sudden profuse painless hemorrhage; pulseless. Not in labor, unpre-

pared closed cervix, diagnosis made of placenta previa, classic cesarean section performed. Placenta found covering the cervical os and lower anterior uterine wall. Patient transfused during operation. In spite of intravenous pituitrin and uterine and vaginal gauze packing, patient continued to bleed. General condition poor. Vaginal packing became blood soaked, was removed and replaced. Intravenous 5 per cent glucose with saline started; adrenalin and caffeine sodium benzoate given as patient appeared exsanguinated. Patient died two hours later in spite of emergency treatment.

Peritonitis.—Primipara, aged nineteen years, admitted after six hours in labor. Membranes ruptured twenty-six hours. After labor of nineteen hours, two fingers dilated; cervix thick, breech presentation, not engaged; two-flap cesarean section performed. Day following operation temperature 103°. Marked abdominal distention. Patient died on the fifth day postoperative with symptoms of peritonitis.

Peritonitis.—Primipara, aged thirty-one years, admitted after eighteen hours in labor; with a justominor pelvis, and the fetus in a transverse presentation. No vaginal examinations done. Membranes ruptured two hours before operation. Classical cesarean section performed. Within twenty-four hours after operation her temperature rose to 103°, and thereafter gradually climbed to 107° on the fifth day, when she died. Postmortem inspection showed evidence of peritonitis (generalized).

Peritonitis.—Primipara, aged twenty-five years, admitted in labor with history of albuminuria and hypertension of two months' duration with generalized edema. After twelve hours of labor, no engagement; membranes intact. Classic cesarean section performed. On third day postoperative, marked abdominal distention. On exploration of wound, found separated with knuckle of gut caught in wound. Intestine replaced and abdominal wall resutured. On twelfth day postoperative, patient's condition poor; taken to operating room, wound reopened and abdomen explored. Uterine incision found gaping and several perforations of small intestine present. Evidence of general peritonitis. Patient received transfusion but died five hours after second operation. In retrospect it would appear that both these patients should have had two-flap extraperitoneal cesarean sections.

Peritonitis.—Multipara, para ii, aged thirty years. Two previous normal deliveries; in labor sixteen hours; membranes ruptured for five hours, position R. O. A.; cervix 2½ fingers dilated, head floating. Low two-flap cesarean section performed. Patient died on seventh day with symptoms of peritonitis (one vaginal examination five hours before operation).

Sepsis.—Primipara, aged twenty-nine years, in labor three days; cervix 3½ fingers dilated; membranes ruptured three days. Two-flap section performed. Uterus was full of meconium; endometrium green and necrotic. No temperature until third day postoperative, then bad chills, followed by temperature as high as 106° to 107°. Repeated blood cultures negative. Three blood transfusions given. Stitch-abscess, suppuration of wound and evisceration followed. Patient continued downhill in spite of therapy, and died sixteen days postoperative. In retrospect this patient's chances of survival would have been increased if she had been delivered by a Porro or Latzko cesarean section.

Psychosis.—Primipara, aged thirty-one years, admitted in sluggish labor with marked psychic disturbance. After thirty-eight hours of labor attended by uterine inertia, no dilatation or engagement was evident. Low cervical transverse cesarean section was performed. On second day postoperative although pelvic condition was satisfactory, patient became violent and had to be forcibly restrained. During the night patient got out of bed and became uncontrollable. Temperature 107°. Psychiatric consultation: toxic exhaustion psychosis. Patient died third day postoperative.

Perforated Peptic Ulcer.—Profuse painless vaginal bleeding six hours after onset of labor. Section performed and placenta found to completely cover the internal os. Moderate febrile convalescence for eleven days. On the twelfth day postoperative patient suddenly vomited large amount of dark red blood. Improved under sedative treatment. Several hours later she suddenly went into shock and died. Autopsy findings: Subacute duodenal ulcer with perforation and erosion of artery; massive gross hemorrhage into intestinal tract and stomach; puerperal gangrenous endometritis and abscess of the right broad ligament.

Pneumonia.—Patient, aged twenty-four years. Primipara with flat pelvis. In labor twenty hours; cervix two fingers dilated; floating head. Under spinal anesthesia, two-flap section done. Examination of chest revealed an extensive lobular pneumonia twenty-four hours later. Patient died on fourth day postoperative. No postmortem.

Pneumonia.—Primipara, aged thirty years, admitted in labor after having 3 convulsions at home. Labor pains for eight hours; one finger dilated; membranes intact. Patient complained of severe dizziness and blurred vision. Became irrational just after admission. Legs markedly edematous. Blood pressure 164/104. Albuminuria present. Classical cesarean section performed under general ether anesthesia. For four days postoperative her condition was fair, with normal temperature, blood pressure 150/80, edema disappearing, and fully rational. On the fifth day she developed signs of a right upper and middle lobe pneumonia. Her condition became worse, and finally coma ensued. Died on sixth day postoperative. No postmortem. In retrospect, it would appear that local anesthesia would have been preferable.

Pulmonary Infarct.—Patient, aged thirty-three years, para ii, gravida iii, admitted after twelve hours of active labor with membranes ruptured for thirty-six hours, and a prolapsed arm. Arm replaced. After twenty-four more hours of labor, the head did not engage. Low two-flap cesarean section performed. For the first three days after the operation, her condition was good. On the fourth day, she developed a pulmonary infarct, and died on the fifth day. No postmortem examination.

Pneumonia.—Patient, aged thirty-six years. Primipara with a history of rickets as a child, and a flat, rachitic pelvis, admitted for an elective cesarean section. Full term, not in labor; membranes intact. Classical section performed under ether anesthesia, which was taken poorly by the patient. On the day following operation, patient developed a temperature of 102.5°, pulse 150, respiration 34, with signs of pulmonary involvement (bronchopneumonia). Temperature kept mounting; course rapidly downhill, and died on fourth day postoperative of pulmonary edema following a fulminating bronchopneumonia.

Ablatio Placentae.—Patient, aged twenty-nine years, para ii, six and one-half months gravid, was admitted to hospital with severe abdominal pains accompanied by vaginal bleeding for four hours; moderate syncope. Abdominal examination revealed a uterus the size of a full-term pregnancy, markedly tense, ligneous in consistency. Fetal heart not heard. Cervix undilated and unprepared. Patient exhibited marked pallor; mucous membranes blanched; pulse rapid and thready. Diagnosis: ablatio placentae. Classical cesarean section. Transfusion on operating table. Patient did not react to intensive stimulation and died nine hours after the operation.

Nephritis Uremia.—Patient, aged thirty years, para iii, a deaf mute, admitted to hospital because of marked edema and dyspnea of one week's duration. Blood pressure 260/150, 3+ albuminuria. Not in labor. Membranes intact. Impression was that of a fulminating toxemia. After twenty-four hours of sedative and eliminative therapy, a classical cesarean section was performed. Living infant. Postoperative course smooth for two days. Pressure dropped to 175/110. On

third day after the operation, developed temperature of 103.4°, restless. Papilledema present. Total urinary output for twenty-four hours was seven ounces. Immediately thereafter she developed a complete urinary suppression and, despite all attempts to stimulate renal activity, died of uremia on sixth day after the operation.

COMMENTS

1. The number of incidental operations has been kept down to the minimum in our belief that it is good surgery not to do more than the cesarean section except in the presence of some urgent indication.

2. We are impressed with the importance of making the necessary decision to intervene in borderline cases before delayed operation with its morbid consequences, both maternal and fetal, nullifies the benefits of this type of delivery.

3. In repeat cases, we favor a moderate trial labor where the preceding operation has had an afebrile convalescence; and the primary indication has not been a bony dystocia precluding the possibility of subsequent vaginal delivery.

4. In our hands the low cervical two-flap operation has given the best results both as to lowest mortality and morbidity. The classic operation has been reserved for elective cases and low placental insertions not long in labor.

5. A recent valuable adjunct has been 0.5 c.c. of pituitary extract diluted with 4 c.c. of warm saline, instilled slowly into the vein in the elbow, as soon as the fetal head is delivered. This causes a prompt, firm contraction of the fundus uteri, with advantages threefold: conservation of the patient's blood, spontaneous separation of the placenta, and a clearer operative field. If given slowly in the above dilution, pituitary shock does not occur.

6. Past experience with unexpected abdominal delivery of a monster emphasizes the importance of a routine x-ray of the abdomen prior to operation.

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A REVIEW OF 226 CASES OF OBSTETRIC ANALGESIA*

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THE present survey of analgesia in obstetric patients is based on intensive study and personal observation during the past ten years. Only cases coming within recent experience, however, are reported in detail in this paper.

The series includes 226 cases drawn from private practice during the past two years (1934 to 1935 inclusive). They are unselected from every standpoint, except that they illustrate the effect of a pento-barbital-scopolamine-nitrous-oxide combination, in various dosages of each. The methods employed represent the outgrowth of experience with various successive types of analgesics, starting with the old twilight sleep formula, in 1925. As each in turn was abandoned, it was replaced by another which seemed to offer greater promise; and it is my earnest hope that a combination will be evolved which will even be superior to the one about to be described.

My purpose in presenting this report consists not only in outlining the general principles upon which the present plan of obstetric analgesia is based and the results obtained—but, more especially, in bringing out in more detail some personal impressions gained through close and constant supervision of the parturient woman.

The success or failure of amnesia in these cases is based upon the patient's own estimate; the classification in every instance being made on the basis of her judgment. Thus, cases were divided into one of three classes: either as "excellent," as "good," or as "failures." The designation "excellent" was applied when complete amnesia was attained in a patient who has no recollection of disagreeable pain. When the patient remembered severe pain, no matter for how short a time, the result was considered "good." A case was regarded as a "failure" when there was no amnesia for the greater part of the labor due to late administration or insufficient dosage.

A combination of pentobarbital-scopolamine and nitrous oxide was used in these cases. The end-results as judged by the patients' testimony were: "excellent" in 91 per cent of the entire series; "good" in 7 per cent; and "failure" in 2 per cent.

Of primary importance in any analgesia is the safety of mother and baby. No method which increases the obstetric hazard is to be tolerated. In this series there was no maternal death.

The infant mortality includes two cases (one for each of the two years), which gives a stillbirth rate of 0.9 per cent for the entire series. The first stillbirth was a case of cervical dystocia in a funnel pelvis,

with a cord wound tightly around the neck, requiring a median forceps after a protracted labor. The second was a case of prolapsed cord. In neither of these cases could the result fairly be laid at the door of the analgesia.

The morbidity in this series, based on a temperature of 100.4° F. for any two days, not on the day of delivery, was 2 per cent. The morbidity based on 100° was 4 per cent. The morbidity was not serious in any of the cases.

The total number of forceps in this series is 57. This gives a forceps incidence of 25 per cent. These were distributed in the following manner: one high forceps, 16 median forceps, and 40 low or outlet forceps.

There were 3 cases of postpartum hemorrhage representing an incidence of 1.3 per cent; one of these patients was given a transfusion.

STUDY OF CASES FOR THE YEAR 1934

For the purpose of more detailed analysis, the year 1934 was studied as a unit. During that year there were 103 cases in which some part, or all, of the pentobarbital-scopolamine-nitrous oxide combination was used. There were 67 primiparas and 36 multiparas. The net result of the analgesia in this series was: "excellent" in 85.4 per cent; "good" in 10.8 per cent; and "failure" in 3.8 per cent.

There was no maternal mortality.

The infant mortality consisted of one case (previously described), a stillbirth rate of 0.9 per cent.

The morbidity in these cases, on the basis of 100.4° F., was 1.9 per cent. On the basis of 100° F. two additional cases must be added to the list, making a total of 4 cases, and a morbidity rate of 3.8 per cent.

The forceps incidence in this group was 35.9 per cent. Of the forceps deliveries 35 per cent were mid-forceps and 65 per cent were low forceps.

During labor, 56 of the 103 patients were examined vaginally, making a total of 74 examinations. Rectal examinations, which were not included in the figures just given, were usually made to determine the progress of the labor.

Episiotomy was done in 63 per cent of these cases.

The condition of the pelvic floor in the remaining 38 cases may be summarized as follows: 22 patients had no tear; 11 had a first-degree tear; and 5 had a second-degree tear.

The blood loss in these cases is of especial significance. The standard used for average bleeding is 200 to 300 c.c., less than average up to 200 c.c., and 300 to 500 c.c. more than average bleeding; beyond that it is described as postpartum hemorrhage. There was one postpartum hemorrhage, or 1 per cent; more than average bleeding occurred in 12.6 per cent; and in 71.8 per cent less than average bleeding occurred.

It is in most instances possible to dispense with inhalation ether during delivery when this method is used. This is an advantage in that it tends to eliminate one of the factors contributing to blood loss.

The influence of this method on the babies was calibrated by two factors: first, the amount of initial asphyxia, and the difficulty of resuscitation, and second, the progress of the infant as reflected by a gain or loss in weight. Breathing was delayed for more than the usual time in only six babies, and a mild form of resuscitation was used. Upon analysis of the weight charts, it was found that 71 per cent of the babies exceeded birth weight on the fourteenth day, and 29 per cent were below birth weight on the fourteenth day. The average gain was 175 gm. above birth weight, and the average loss, 130 gm. This type of analgesia has no effect on the immediate or remote course of the infant.

METHOD

The average first dose of scopolamine was $\frac{1}{150}$ gr., given in conjunction with an average first dose of pentobarbital of $4\frac{1}{2}$ gr. The average character of the pains when this first dosage was given consisted in contractions at an interval of four to five minutes, and having a duration of thirty to forty seconds. The average interval between the first and second dosages was $2\frac{3}{4}$ hours for primiparas and $1\frac{1}{4}$ hours for multiparas. The average second dose was $\frac{1}{200}$ gr. of scopolamine, and $4\frac{1}{2}$ gr. of pentobarbital. In prolonged labors, when a third dose was necessary, it averaged $\frac{1}{200}$ gr. of scopolamine and 3 gr. of pentobarbital.

The various dosages were distributed in the primiparas as follows: One dose was required in 34 per cent; two doses were given in 50 per cent; three doses were required in 15 per cent.

The multiparas required the following dosages: 80 per cent were given only one dose; 17 per cent were given two doses; and 3 per cent required three doses.

An effort was invariably made to individualize the patient, as far as the dosage was concerned. The dosage varied anywhere from one capsule ($1\frac{1}{2}$ gr.) of pentobarbital to six capsules (9 gr.) and $\frac{1}{250}$ to $\frac{1}{100}$ of a grain of scopolamine. All patients were tested before labor with pentobarbital to see if there was any idiosyncrasy to the drug but none was found.

ADVANTAGES AND DISADVANTAGES OF OBSTETRIC ANALGESIA

The foregoing results, I believe, compare favorably with the average similar private group in which analgesia has not been employed. However, these results do not convey any adequate idea of the difficulties encountered in their attainment. Published accounts of analgesia statistics with which I am familiar give the impression that the results are universally good if a certain set of drugs is administered in a more or less routine fashion. This has not been my experience. I have found it a very laborious and exacting task, and the more perfect the amnesia, the more laborious and exacting it becomes.

I would like to indicate some of the features which seem to me to be important in attaining a good result and I want especially to emphasize some of the potential disadvantages of the method.

At the outset, let us take the most burdensome feature, namely, the necessity for the constant presence of the obstetrician. This is of course a primary disadvantage, but it is my conviction that it is very essential to successful analgesia. So numerous are the factors requiring his personal interpretation, that his presence is imperative. I have been consistently unsuccessful in the "remote control" of analgesia.

To illustrate how this is linked up with the process I will point out one important feature in this work, namely, the psychic attitude of the patient. An agreeable, relaxed, fearless mental state as opposed to a tense, fearful one is desirable before the first dose is given. This can be best attained through the reassuring presence of her physician. She is not so likely to fight the sedative, there is less fear, and the drug is more successful in its effect.

Another important feature is the postponement of the first dose. To neutralize perhaps the greatest handicap of this form of analgesia, namely the slowing of labor by the depression of the force of and the lengthening of the interval between the uterine contractions, one must be particularly cautious with the first dose. It has been reported that pentobarbital accelerates the first stage of labor. It has been my experience that pentobarbital or any sedative, given too early in labor, will lengthen the period between contractions and prolong the labor. For this reason it is desirable to delay the administration of the first dose, especially in primiparas, to an optimum point of rhythm and intensity of the pains, but not to a point of severe discomfort. Each patient offers an individual problem in her reaction to pain; but all have this common denominator, that if they know complete relief is available and theirs for the asking, and that their consciousness of these pains has a limit which is more or less in their hands, they are content to endure them for a longer time, without complaint, than they otherwise would. In this way the doctor is not stampeded into giving an early initial dose.

The problem of initial dosage in the average case is not so much a question of amount. as a question of time. In the primipara with plenty of time ahead of her, and with slowly developing pains, the first dose should effect some sedation but, more important, it should lay the groundwork for the doses to follow. In the multipara, who is more expeditious in her work, the object of the first dose is to effect amnesia, if possible, before the development of strong pains. The amount of the first dose is therefore usually larger for the multipara than the primipara and is also given earlier.

An examination of the patient at this juncture is in order. Information on two important points is essential, namely, what the patient is doing at the moment; and second, what you may expect her to do in the immediate future. The former concerns the initial dose; the

latter has to do with subsequent doses, and their relationship to the first. By examination, I refer to vaginal examination.

Since time is the important feature in analgesia, by the same token, the evaluation of the resistance to the advancing part and the amount of energy being developed to overcome this resistance are equally important. The cervix and the contraction tell the greater part of the story. When the cervix is long and thick, it is best to postpone the first dose until there is some retraction and dilatation.

Individual pain reaction to the same mechanical force is a variable entity. Both the contraction and the complaint must be taken into consideration. But if the contraction is feeble and the complaint great, a smaller dose is advisable.

In spite of careful supervision, delayed labor due to analgesia may occur. Then it becomes necessary to stimulate labor, maintaining the narcosis. Nothing is more discouraging for a patient than to wake up and to realize that the worst is ahead, rather than behind her. If a mistake has been made and the labor definitely slowed, there are three ways in which it can be stimulated: (1) by small doses of pituitrin (usually two minims); (2) by rupture of the membrane; and (3) by flexing the extended head. All of these methods are not without hazard. If the first dose is given at the right time, these procedures will not be necessary. The following procedure is of great value in expediting labor when it has been delayed by too early or too much analgesia: The patient is placed in the extreme lithotomy position, the head is flexed to as great a degree as possible, and at the same time an attempt is made to push it downward and backward toward the hollow of the sacrum. This in many instances corrects the direction of the force and, in so doing, renders the contraction more efficient, and may considerably reduce the time of labor. Induced labors offer the highest potential for delay by analgesia. In cases where pelvic dystocia is expected, one should be cautious in administering the first dose.

Once the analgesia has been established, it should be maintained until after delivery. It is the maintenance of this state that calls for successive doses. It is sometimes difficult to tell whether or not the patient is conscious. Incoherence of speech or thought, even though occasionally interspersed with rational conversation, usually indicates that there will be no subsequent memory of the labor. When it is suspected that the analgesia is not complete, it is occasionally advisable to anesthetize the patient with nitrous oxide. This should be given continuously, over a period of from five to ten minutes. Outside stimuli are cut off from the patient by this means, the effect of the sedative is reinforced, and prolonged analgesia results. Advantage may be taken of this nitrous oxide administration for an examination.

Restlessness is one of the great disadvantages of this method of analgesia. Pentobarbital may be increased without the scopolamine, which tends to quiet the patient. Occasionally, in cases of extreme restlessness, rectal ether may be used with good results. Competent nursing supervision is always essential, both before and after delivery, until the patient is completely awake. This, of course, complicates the nursing problem, but it is a virtue in another direction, in that it insures continuous care of the patient.

In this entire series there has been but one injury. One patient bruised her lip. That was the extent of the self-inflicted trauma.

The time of delivery is the point at which restlessness becomes a personal problem for the obstetrician. There is a tendency to control this with complete narcosis and to terminate labor with forceps. This is unnecessary, as the patient can be restrained on the table, with the use of a small amount of nitrous oxide. There is no diminution in the natural expulsive forces during the second stage.

In order to determine the validity of this belief, an effort was made, in 1935, to allow as many cases as possible to terminate spontaneously. The necessity of employing forceps dropped from 35.9 per cent in 1934 to 16 per cent in 1935. The use of low forceps in these cases is a concession to the peace of mind of the operator, and not a necessity for the patient.

An increase in the tendency toward asphyxia of the baby is popularly ascribed to this procedure. It should be emphasized that nothing of this nature was observed in any case in the series. In fact, no deleterious effects were noted in cases in which the terminal dose was given just before delivery. The babies flourish and gain in the postpartum period, and the likelihood of their having brothers and sisters at an early period is an attribute of analgesia which should not be disregarded.

This series will illustrate the obstetric results that may be obtained coincidentally with successful analgesia. Obstetricians seem to be divided into two classes: those who do not use analgesia, and those who use it and write about it. The former are extravagant in their criticism; the latter, in their praise. The former believe that analgesia retards and complicates labor, the latter insist that the reverse is true. I would like to place myself somewhere between the two groups. The fact should be emphasized that, above all, this method calls for individualization of the patient, each one being regarded as a distinct clinical unit. It will be noted that no attempt has been made to standardize either the dosage or the time intervals, for the reason that no general rules are possible in this connection. The successful administration of these drugs requires the constant presence and taxes the skill of the most experienced in this field. The ultimate object is the creation of complete amnesia without affecting the course of labor.

This is in most instances no simple feat. While probably no one will doubt the possibility of attaining complete amnesia, its accomplishment, unattended by disagreeable features, is a goal which one can hope to attain only as a result of infinite patience combined with considerable experience.

To summarize briefly the important conclusions:

1. Perfection in analgesia has not been attained.

2. Individualization of each patient is essential.

3. Constant medical and nursing supervision is imperative.

4. Each patient should be tested for idiosyncrasy to the drug before labor.

5. Restlessness can be a disagreeable feature of this analgesia.

6. Blood loss is not increased by this method of analgesia.

7. The length of labor need not be increased by this analgesia.

8. Forceps incidence need not be increased.

9. Mental trauma is definitely decreased.

10. In the hands of a competent obstetrician it is a safe analgesia for mother and baby.

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DISCUSSION

DR. GEORGE H. RYDER.—Amnesia in labor has been attained by Dr. Damon in 91 per cent of his cases. This is a high percentage, and it has been attained with no maternal loss and with a very low fetal mortality. In a larger series it is conceivable that such nearly perfect results might not hold. His incidence of forceps operations, 25 per cent, is not high for private patients, more especially when 70 per cent of the forceps were of the low variety. His incidence of postpartum hemorrhage, 1.3 per cent, is also not unduly high.

I do not believe, however, that amnesia in labor is the goal for which obstetricians are striving. Rather is it *painless* labor. This is not the loss of memory of pain, but rather no pain to remember. These patients with amnesia probably suffer as much as or more than those delivered in other ways. It is simply that they forget the pain they have had. I wonder what effect pain has on the nervous systems of patients temporarily deranged mentally. Possibly none. But we do not know.

There are serious disadvantages to amnesia during labor. Dr. Damon mentions the extreme restlessness and excitability, calling for constant surveillance and restraint. In one unguarded moment on the part of an attendant, the patient may jump out of the window or do herself other bodily harm.

Already we have at hand many measures for easing the pain, none ideal, but many nevertheless very helpful. Morphine is a drug too little used. It has been demonstrated recently that morphine does not diminish uterine contractions and therefore it should be a most useful drug in labor, for it certainly does lessen pain. Morphine, $\frac{1}{4}$ gr., early when the pain is becoming troublesome, is most helpful, and in long labors it may be repeated safely. It does not harm the fetus unless given just before birth when it may depress the respiratory center.

Analgesia in labor has come to stay. It is a product of civilization. Wisely used, it does not increase maternal mortality, nor fetal mortality. Nor does it add to birth injuries or fetal damage, or cause an increase in operative interference.

DR. ALBERT H. ALDRIDGE.—On the service at the Woman's Hospital, we are using routinely the same combination of drugs and in practically the same dosage which Dr. Damon has employed in the series which he has just reported.

I agree with Dr. Damon that success and safety in the utilization of analgesic drugs during labor depend upon testing a patient before the onset of labor to detect a possible idiosyncrasy to the drugs to be used; on gaining the confidence of the patient during the antepartum period and early hours of labor; on avoidance of any medication until labor is well established; on the selection of proper dosage of drugs to fit the type of labor and on the careful study of the patient's reaction throughout labor. If these precautions are observed analgesic drugs in adequate dosage may be used routinely during labor with safety to the mother and baby, and without disturbing the normal processes of labor.

Dr. Ryder has referred to possible undesirable after-effects on the personality of patients who have been temporarily deranged by use of drugs which cause amnesia and analgesia. It is our impression, however, that the satisfactory postpartum condition and rapid convalescence of patients who have been spared fatigue and mental trauma of labor is the most convincing evidence against such criticism and of the value of such drugs to the mother.

DR. JOHN E. TRITSCH.—I agree that when we speak of obstetric analgesia we are usually referring to obstetric amnesia. When we arrive at the perfect analgesia, we will have arrived at something that actually eliminates pain, not merely the recollection of pain. To accomplish this we shall have to devise some means by which the sensory fibers coming from the uterus will be paralyzed, whereas the sympathetic fibers which produce contraction, as well as the local contraction initiating centers in the uterus, will be uninfluenced by the treatment. We have used the barbiturates with scopolamine at the Fifth Avenue and Metropolitan Hospitals many times and have failed to produce analgesia, so that, as a consequence, we are now more inclined toward the use of rectal ether with the barbiturates. We have been using the acid form of the barbiturates, as, for example, amytal, pentobarbital and allurate in the acid form, which dissolve in ether, with which we think we get a little more uniform absorption of the substances. We feel also that we control the excitation which has been referred to, to such a degree, that we practically never have any patients who are excited sufficiently to cause trouble. However, we still have occasionally a patient who is partially anesthetized and consequently must be constantly watched.

I noted that in Dr. Damon's experience, the duration of the action of the drug in primiparas was two and three-fourth hours and in multiparas one and one-fourth hours, which required repetition of treatment in many cases. With the barbiturates in ether the necessity for repetition is very rare. In almost all of our cases we get six to eight hours of analgesia and the necessity for repetition has occurred only two or three times in a series of several hundred cases.

In primiparas the longer acting barbiturates will probably be more desirable and the shorter acting ones in the multiparas. We have recently been experimenting with evipal rectally, in combination with rectal ether, and found that we got about three or four hours of analgesia. We got six or eight hours with the longer acting barbiturates. Pentobarbital falls in a class between evipal and the longer acting drugs, such as amytal and allurate. When we used evipal in primiparas, the patient frequently came out of the analgesia long before the time of delivery, whereas, when we used it in multiparas, the action was sufficiently long to accomplish the desired result. So we feel that investigation, as far as parity and expectancy of time of delivery, is an important element.

We also feel that the multiparas have to a certain extent been neglected in connection with our attempts at alleviating labor pains, primarily because of the fact that they frequently have precipitous labors. To patients who come to the hospital just about ready to deliver we just give nitrous oxide. The use of nitrous oxide in the second stage of labor is a prerequisite to the satisfactory relief of pains of labor, while the analgesics and amnesics are primarily for use in the first stage.

FURTHER OBSERVATIONS WITH DIAL URETHANE FOR OBSTETRIC ANALGESIA

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IN OCTOBER, 1934, a preliminary report was made on the use of dial urethane solution for obstetric analgesia.[2] The results up to that time had been very satisfactory, but the limited number of cases in which the preparation had been used rendered caution necessary in drawing conclusions. In the two years that have elapsed since the submission of this report, the opportunity has occurred to employ the solution in 198 cases more, so that the series now numbers 254. The additional experience gained during this time has served to strengthen certain of the earlier impressions gained, but has led me to modify some of the views expressed in the preliminary paper. Because of these facts, it was felt that a supplementary report might possess sufficient interest to justify its publication.

As previously explained, the dial urethane solution contains 10 per cent dial (diallyl-barbituric acid) and 40 per cent urethane, and is available in 2 c.c. ampules. Obviously, to refer to it merely as ''dial'' is incorrect, because the urethane present must contribute something, at least, to the action. Intravenous administration has been employed in all the cases forming the basis for this report. That this method of administration is essential for truly effective analgesia, I am convinced by my own experience with intramuscular injection, and also by the indifferent success following intramuscular injection as reported by McNeile and Vruwink[9] and by Rund.[13] It is true that a certain element of danger is always present when intravenous injection is practiced, but that this danger is sufficiently great to render unwise the careful and intelligent intravenous injection of the dial urethane solution has certainly not been indicated by my experience nor, apparently, by that of any other authors who have employed it in obstetric patients. I cannot, however, too strongly emphasize the necessity of scrupulous care in carrying out the injection; it is not a procedure that may be safely delegated to nurse or inexperienced interne, but should be made by the obstetrician himself or under his direct supervision.

The question of correct dosage is, of course, of great importance. The first consideration is the safety of the patient, but, while keeping this always in mind, one should avoid the mistake of so limiting the dose that satisfactory analgesia consistently fails to develop. In my first cases, the dosage recommended by Nelson[11] was employed. Satisfactory results were obtained in a certain proportion of the cases, but failure so often occurred that I soon became convinced that larger amounts of the solu-

tion were frequently necessary. Birnberg and Livingston,[1] likewise, found Nelson's dosage insufficient, stating that "all patients required at least 4 c.c. before any appreciable effect was seen"; because of which they arbitrarily adopted 4 c.c. as initial dose, regardless of weight or other individual peculiarities. As regards subsequent administration of the solution, these authors attempted some individualization, considering no further injections necessary if delivery occurred within an hour after the first dose and omitting the third injection "if the patient was markedly narcotized after two doses." Weight, too, according to them, should be given due consideration: patients of 125 pounds or less receiving only 2 c.c. in second or third injections, while those weighing 170 pounds or more received routinely 4 c.c.

The maximum narcotic effect of dial develops almost immediately after entrance of the drug into the blood stream. Taking advantage of this fact, Garcia[3] employed what was subsequently designated by Holtermann[4] as "biological dosage," injecting the solution intravenously at a slow rate until the patient lapsed into unconsciousness. Although unfamiliar at that time with the work of Garcia and Holtermann, it soon became evident to me that individualization in dosage was not only desirable but actually necessary if satisfactory analgesia was to be secured and, at the same time, the safety of the patient taken into consideration. Weight, alone, is not a safe guide in determining dosage. As a general rule, the heavier the patient, the larger the effective (and safe) dose of dial urethane: this is far from being invariably the case; indeed, I have found that not infrequently the larger patients are of a more phlegmatic type and respond more readily to the action of the preparation than is sometimes the case with smaller, highly nervous individuals. A technic was soon developed, which is still adhered to so closely that the description given in my earlier report may be quoted in full:

The patient is told that she will feel relaxed and sleepy from the injection; a matter of some importance, because, otherwise, alarm may be experienced over the peculiar sensation. Four cubic centimeters of the solution are drawn up into a 5 c.c. syringe and the needle thrust through the vein wall. Injection is made slowly, the patient being constantly questioned and the injection discontinued when she no longer responds. In some cases, 2 c.c. of the solution will suffice; in others, it may be necessary to inject the full 4 c.c.; I have never given in excess of this latter amount in any single injection. If sound sleep does not occur between pains, a second injection of 2 c.c. is given in thirty minutes. Further injections, each of 2 c.c., may be given, but I have not exceeded a total of 8 c.c. in the course of any labor.[2]

With added experience, I have become convinced that it is sometimes desirable and also safe to increase the dose above the limits set in the preliminary report, both for initial and total injections. This conclusion has not been arrived at hastily; it has been rendered possible by considering various published reports on the dosage of the solution and also by carefully feeling my way, slightly increasing the volume injected in

"refractory" patients, with constant careful observation of the immediate and possible delayed reaction in such cases.   Again let me emphasize the need for scrupulous care in selection of dose and in attention to technic of administration: it must always be borne in mind that active drugs are being introduced directly into the circulation and one should not forget the disastrous results that followed the reckless advocacy of enormous doses of another barbiturate intravenously for the induction of surgical anesthesia.   My earlier limitation of 8 c.c. for total dosage was set because of the reported experience of Nelson,[11] Hoven,[5] and Muller.[10] The first mentioned of these authors found that it was seldom necessary to equal this dosage in obstetric patients; and Hoven and Muller, from their observations on the use of dial urethane for "narco-sustained therapy" in insane patients, considered it unwise ever to exceed a total dosage of 8 c.c. during the course of twenty-four hours.   However, not only I found Nelson's dosage often inadequate, but Birnberg and Livingston,[1] as previously mentioned, came to a similar conclusion.   Regarding Hoven and Muller's papers, it should be borne in mind that conditions present in cases under narco-sustained therapy are vastly different from those to which the parturient woman is subjected: in the former, a state of partial or complete narcosis exists for several days; moreover, these insane patients are given fairly large doses of scopolamine along with the dial urethane.   In rare instances it may be advisable to inject more than 4 c.c. for the initial dose in obstetric patients; however, this should be done only when the individual has failed to respond to the former maximum of 4 c.c. *when injected at a rate not to exceed 1 c.c. per minute*.   Observing the precautions that have been stressed, I have never encountered an instance of either respiratory or circulatory depression in the sense generally used, nor have I seen any cases where late results attributable to the unfavorable influence of the medication were present. Birnberg and Livingston,[1] also, observed no deleterious effects after initial doses of 6 c.c. and total doses of 12 c.c. although it is my belief that their fixed-dosage method is less dependable and not as safe as the elastic one employed in my series.

The criteria for judging the effectiveness of the dial urethane solution have been analgesia and amnesia.   Analgesia is graded as good, fair, or poor: amnesia as complete, incomplete, fair, or absent.   The only disadvantage, from the maternal standpoint, so far encountered has been restlessness, either mild or amounting to actual mania; while, as regards the infant, the only undesirable effect of the medication clearly established is that occasionally involving the respiration.

Of the 254 patients, one was given a total of only 3 c.c. of the dial urethrane solution, with good anesthesia and complete amnesia; however, the patient was para iii and labor lasted only three hours. Seven patients were given a total of 4 c.c., with good analgesia and complete amnesia in six instances, and fair in the seventh. A total dosage of 6 c.c. was employed in 22 patients, with good analgesia in 20, fair in 1, restlessness in 1, complete amnesia in 19, and fair in 3. With a

total dosage of 8 c.c. in 79 patients, good analgesia was obtained in 63; fair analgesia in 13, poor analgesia in 1, complete amnesia in 77, fair amnesia in 1, no amnesia in 1, mild restlessness in 1, and mania in 1, this being the only case in the series that was maniacal and required physical restraint. Eighteen patients were given a total dosage of 9 c.c. with good analgesia in 17 and fair in 1; amnesia was complete in all, and there was no instance of restlessness recorded. The total dosage of 10 c.c. was given to 95 patients, analgesia was good in 83, fair in 6, and poor in 1, while amnesia was complete in 92 and fair in 3. Restlessness was noted in 5 patients after this dosage. After a total dosage of 12 c.c. in 31 patients, analgesia was good in 24, fair in 3, and poor in 1, while amnesia was complete in all and restlessness was noted in 3 cases. One patient, a primipara, was given a total of 14 c.c. during the course of a thirty-six-hour labor, with good analgesia and complete amnesia. Engagement not having occurred at the expiration of this time, section was performed and a posterior fibroid, large enough to prevent entrance of the head into the pelvis, was found. Although the patient took food and water during labor, she had no recollection of events occurring during labor, including her transfer to the operating room and administration of inhalation anesthesia.

Analysis of my data reveals the interesting fact that results were independent of the size of the dose of dial urethane employed. Thus, after a total dosage of 4 c.c., good results were obtained in 85.7 per cent of the cases; after 6 c.c., in 90.9 per cent; after 8 c.c., in 78.4 per cent; after 9 c.c., in 94.4 per cent; after 10 c.c., in 87.3 per cent; and after 12 c.c. in 77.4 per cent.

This serves to stress the fact that elasticity in dosage, allowing individualization, is most important, because by means of its intelligent application one is able to avoid the danger of needlessly administering large amounts of the analgesic and, at the same time, is reasonably sure of obtaining effective analgesia and amnesia. My experience establishes, I believe, that it is unwise to adopt any fixed rule for dosage that should apply to every individual, regardless of constitutional differences: the dose should be adapted to the individual, but should rarely exceed 4 c.c. at the first injection or 12 c.c. as total amount during the labor. I should certainly feel considerable hesitation about giving an initial injection of as much as 6 c.c.; fortunately, none of my patients has been so refractory as to require more than 5 c.c.; indeed, as already mentioned, in practically all cases, 4 c.c. or less will suffice as initial dose.

Obviously, physicians and patients both will vary in their estimation of the efficacy of an analgesic. When a patient rests quietly between pains and merely moves slightly and moans while the uterus is contracting, I have considered analgesia as "good," but only "fair" if she is conscious and talkative in the interval during pains. Restlessness deserves especial consideration; I have classed it as "mild" if the patient moves constantly or intermittently in the absence of pains. However, it should be borne in mind that the patient under the influence of an effectively analgesic dose of dial urethane should never be left alone for a moment, but should constantly be under the supervision of a responsible attendant, preferably a physician or trained nurse. These patients are, at best, semiconscious, and one never knows when they may roll out of bed, or, indeed, develop mania, although this latter

occurred in only one of my series. In my earlier report,[2] approving reference was made to the condemnation by Irving, Berman, and Nelson[6] of opium derivatives as obstetric analgesics, but in the short time that has elapsed since then, I have come to modify my views on this point to a certain degree. While still feeling that opium derivatives are absolutely contraindicated in the multiparous patient and also in the later stages of labor in primiparas, I now am of the opinion that in the exceptional, nervous, apprehensive primipara, just the one who is likely to respond least favorably to dial urethane medication, the *early* administration of a third or even two-thirds of a grain of pantopon exercises a most beneficial effect and, apparently, is most serviceable in preventing the later occurrence of restlessness. This is in harmony with the observation of Birnberg and Livingston[1] that very small doses of morphine (gr. 1/20 to gr. 1/12) prevented excitement and restlessness in their patients who had received dial urethane.

As to respiratory depression of the infants from the action of the dial urethane solution, this is rarely of a severe nature. In the 254 deliveries, there were three pairs of twins, making a total of 257 infants, two of whom were stillborn, but both had apparently died some time before onset of labor, maceration being present. In the remaining 255 infants, spontaneous respiration occurred without delay in 220; 25 infants showed mild depression of respiration; and 10 required rather active measures for resuscitation. As brought out in the recent excellent paper by McGrath and Kuder,[8] haste and overzealous therapy should be avoided in these infants. Care should be directed toward removal of mucus, amniotic fluid, or other foreign material from the air passages, either through postural drainage or, when necessary, by actual suction. The character of the heart action is a far better guide as to the gravity of the condition than the color of the skin or the length of time before respiration starts. It should be borne in mind that artificial respiration, when necessary, must be performed with care; "even mouth to mouth breathing may inflict serious injury." My experience with coramine as a respiratory stimulant in the severer cases of depression has been particularly happy. When clearing out the air passages, mild cutaneous stimulation and careful artificial respiration have not been successful in establishing natural breathing; ½ c.c. of coramine injected into the umbilical vein has, invariably, proved effective. The possibility of overexcitation of the central nervous system by this dosage, suggested by McGrath and Kuder,[8] has not been established by my experience, and instead of manifesting the depressing action of lobeline on the circulation, pointed out by Moncrieff and others, coramine acts as a circulatory "stimulant," as indicated by the improvement in the character of cardiac action and in the color of the skin almost immediately after intravenous injection. Both the safety and the efficacy of coramine when used for respiratory stimulation are estab-

lished, not only by my rather limited observation but by the much more numerous clinical data presented in the papers of Wood,[14] Reese,[12] and Lundy[7] in this country and by a large number of foreign authors. However, I subscribe fully to the statement by McGrath and Kuder[8] that "no drug therapy provides the fundamental clearance and patency of the air passages."

Few additional comments are necessary. Added experience has strengthened the belief that dial urethane analgesia generally hastens cervical relaxation and shortens labor, although rare instances are encountered where the reverse seems true. I have had no reason to alter the earlier expressed opinion that this form of analgesia is *not* contraindicated in the presence of respiratory tract infection; I have employed the preparation in ten such cases with very satisfactory results and no apparent deleterious effects. Delayed recovery of consciousness has not been an inconvenience in my series; even during labor, it is generally possible to rouse the patients sufficiently to have them take liquids.

Dial urethane is not the ideal obstetric analgesic; its safe and successful employment demands an exacting technic and constant supervision of the patients; preferably, within a hospital. Success does not invariably result even when these conditions are complied with, but it has certainly proved the most generally satisfactory agent with which I have had experience. Respiratory depression of the mother has not been encountered, and in the comparatively few instances where this occurred in the infants, clearing out the air passages, mild cutaneous stimulation, carefully performed artificial respiration, and intravenous injection of 0.5 c.c. of coramine, alone or combined, have been successful in every instance.

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TUMORS OF THE OVARY

A Study of 1,101 Cases of Operations for Ovarian Tumor

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THIS paper presents an analysis of laboratory and clinical data from 1,101 cases of ovarian tumor operations performed at the Mount Sinai Hospital during the period from 1924 to 1935. The facts, derived from tables too extended for publication, are at variance with textbook concepts in many instances. These are of interest to the clinician and surgeon.

The tumor types are differentiated by pathologic classification; records without microscopic reports have not been incorporated in this study. Small groups of endometriosis of the ovary and tuboovarian cysts have been included, since the ovary was completely involved.

The frequency of benign tumors as well as carcinomas and sarcomas is given. Age groups by decades are presented in order of tumor incidence and tumors of the first, second, and third frequency are noted. Conversely, tumors are considered from the standpoint of incidence in all decades.

Uterine bleeding, dysmenorrhea, and menopause are studied in relation to the various tumors.

Metastases found at operation indicate the belated onset of symptoms and the foci are grouped by location in body systems. Complications of malignancies are discussed.

Symptoms, grouped under body systems, indicate that almost any abdominal condition may be simulated. The relation between the site of the pain and the site of the ovarian tumor has also been determined. Sedimentation rates are considered briefly.

Neither syphilis nor actinomycosis are found in this series.

The need for a single complete, organized statistical study is indicated by the absence of such a report from the literature.

I. INCIDENCE OF EACH TYPE OF OVARIAN TUMOR (TABLE I)

A. *Common Types.—Simple Cysts:* The 522 cases of simple cysts constitute 47 per cent of all ovarian tumors (1,101). These are the most frequent tumors of the ovary and are made up of follicular (76 per cent) and corpus luteum (24 per cent) cysts.

The follicular cysts are pathologically reported as hydrops, cystoma, follicle cysts, microcystic ovary, simple cystadenoma, and fibroepithelial cysts.

Eight per cent of all simple cysts contain intracystic hemorrhage, 80 per cent of these cases are found in corpora lutea cysts.

Intracystic hemorrhage takes place in 29 per cent of corpora lutea and in only 3 per cent of follicle cysts.

Dermoid Cysts: Although second in order of frequency, this tumor shows an incidence of 31 per cent less than the simple cysts. There are 182 tumors representing an incidence of 16 per cent.

Two of these tumors (1 per cent) revealed malignant change arising from the squamous cell epithelial structures within.

Papillary Serous Cystadenocarcinoma and Cystadenoma: It is significant that this ovarian cancer occupies a position of such high incidence. It is third in order of frequency and comprises 152 instances or 14 per cent of all ovarian neoplasms.

The benign form of this growth occurs four times less frequently; namely, 36 instances among all tumors, or an incidence of 3 per cent. This suggests the insidious nature of these growths and in most cases that recognition occurs after malignant change has set in.

TABLE I.   INCIDENCE OF OVARIAN TUMOR TYPES IN 1,101 CASES

A. Common types:		1,063	
Simple cysts	522		47%
396 follicular			
126 corpus luteum			
Dermoid cysts	182		16%
Papillary serous cystadenocarcinoma	152		14%
Papillary pseudomucinous cystadenoma	64		6%
Endometriosis of the ovary	43		4%
Papillary serous cystadenoma	36		3%
Tuboovarian cyst	29		2.6%
Fibroma	24		2%
Papillary pseudomucinous cystadenocarcinoma	11		1%
B. Rare carcinomas		19	1.7%
Colloid or Krukenberg tumors	6		
Medullary carcinoma	6		
Carcinosarcoma	1		
Solid carcinoma	3		
Squamous cell carcinoma in a dermoid cyst	2		
Undetermined carcinoma	1		
C. Sarcomas:		9	0.8%
Spindle cell sarcoma	1		
Fibrosarcoma	4		
Round cell sarcoma	1		
Hemangiosarcoma	2		
Angiosarcoma	1		
D. Embryonal tumors:		10	1.0%
Teratoma	8		
Disgerminoma	2		
Total		1,101	

Papillary Pseudomucinous Cystadenoma and Cystadenocarcinoma: These tumors are infrequent. The benign form was found in 64 patients, an incidence of 6 per cent, and the malignant form occurred 6 times less frequently, namely, in 11 patients, or an incidence of 1 per cent.

Early reports on the benign pseudomucinous tumors reveal a high incidence. The wide variance between old and recent reports may be due to present routine microscopic examination of tumors.

Serous ovarian tumors are 2½ times more frequent than the pseudomucinous growths. The papillary serous cancers are 14 times more frequent than pseudomucinous cancers but the benign serous growth is found only half as frequently as the benign pseudomucinous tumors.

Endometriosis of the Ovary and Tuboovarian Cysts: Forty-three instances of endometriosis represent 4 per cent of all ovarian tumors.

Tuboovarian cysts, 29 in number, constitute 3 per cent of all ovarian tumors.

These small groups are included because the ovary was sufficiently involved to warrant surgical removal.

Fibroma of the Ovary: This growth was found in 2 per cent of all ovarian tumors; 24 patients were operated upon.

B. *Rare Carcinomas*:   nineteen tumors constitute 1.7 per cent of all ovarian growths. These are made up of 6 colloid or Krukenberg tumors and 6 medullary growths, 3 solid carcinomas, 2 squamous cell carcinomas arising within dermoid cysts, 1 carcinosarcoma and an undetermined malignancy.

C. *Sarcomas*:   Less than 1 per cent of all ovarian tumors are sarcomas. In this series, only 9 were found; 4 fibrosarcomas, 2 hemangiosarcomas, and 1 each of spindle cell, round cell, and angiosarcoma.

D. *Embryonal Tumors*:   In this group are 10 tumors, constituting 1 per cent of all ovarian growths. There are 8 teratomas and 2 disgerminomas. Several of the former were recorded as teratoblastomas.

II. THE INCIDENCE OF OVARIAN MALIGNANCY (TABLE II)

There was 17.3 per cent malignancy among 1,101 ovarian tumors; 16.3 per cent were carcinoma and 1 per cent were sarcoma, representing 191 cases in all.

TABLE II. INCIDENCE OF MALIGNANCY OF THE OVARY

(IN ORDER OF FREQUENCY)

TYPE OF MALIGNANT GROWTH	NO. OF CASES	PER CENT OF MALIGNANCIES
Papillary serous cystadenocarcinoma	152	80.0
Papillary pseudomucinous cystadenocarcinoma	11	5.8
Colloid (Krukenberg) carcinoma	6	3.0
Medullary carcinoma	6	3.0
Fibrosarcoma	4	2.0
Solid carcinoma	3	1.6
Squamous cell carcinoma in a dermoid cyst	2	1.0
Hemangiosarcoma	2	1.0
Other rare sarcomas	5	2.5
Spindle cell sarcoma		
Round cell sarcoma		
Carcinosarcoma		
Angiosarcoma		
Total number of malignancies in 1,101 ovarian tumors	191 or	17.3%
Carcinomas 180—16.3%		
Sarcomas 11— 1.0%		

One hundred and fifty-two papillary serous cystadenocarcinomas represent 80 per cent of all malignant ovarian tumors. This growth is third among all ovarian growths and is 14 times more frequent than the pseudomucinous carcinoma, which was found only 11 times, an incidence of 5.8 per cent. The benign form of the latter is 6 times more frequent.

Both medullary and colloid cancers total 6 instances each, or 3.2 per cent of all ovarian malignancies. Various types of sarcomas range from ½ to 2 per cent incidence among malignancies; the fibrosarcoma, 4 in number, is most frequent.

Cancer and Sarcoma Incidence Among Malignancies: 95 per cent of malignancies are carcinoma, and 5 per cent sarcoma. There were 181 and 10 cases, respectively.

IIIA. AGE INCIDENCE AMONG OVARIAN TUMORS

Simple Cysts.—(522 cases.) Most of these tumors were found in patients between thirty and forty years of age. There were 189 patients representing 36 per cent of all simple cysts. There were 162 patients, or 31 per cent, in the twenty- to thirty-year age group, and 81 patients or 15 per cent were between forty and fifty years. Thus, 82 per cent of simple cysts occur between the ages of twenty and fifty years.

In young women between ten and twenty years of age, there were 77 instances, or 14 per cent incidence of simple cysts, among which corpora lutea, principally, constituted the pathologic findings. Sixty-five of these patients, namely 90 per cent, were young women of early menstrual age between ten and sixteen years.

Forty-four per cent of all simple cysts were found in patients under thirty years of age. The oldest patient in the group was sixty-nine years of age and the youngest twelve years of age.

Dermoid Cysts.—(182 cases.) The largest number, namely forty per cent of these tumors, is found in the third decade. Next in frequency is the thirty to forty-year age group, in which 55 patients, or 30 per cent of all dermoid cysts were found. The fifth decade shows 24 instances, or 13 per cent incidence. Thus, 83 per cent of dermoids are found in a combined age group between twenty and fifty years. The youngest patient was two years old; the oldest was seventy years of age.

Papillary Serous Cystadenocarcinoma.—(152 cases.) This tumor is found principally in women between the ages of forty and fifty years. Thirty-six per cent, or 55 patients, were operated upon. The sixth decade, fifty to sixty years, shows forty such tumors, or 26 per cent incidence, and the thirty- to forty-year age group shows a 22 per cent incidence or 34 cases. Thus, 84 per cent of these tumors occur in patients between the ages of thirty and sixty years. It is the most frequent type of malignancy of the ovary. This growth predominates over all other tumors in the seventh decade: 6.5 per cent or 10 tumors are found. A patient twenty-four years of age was found to have this ovarian cancer; the oldest patient was seventy years of age.

Papillary Pseudomucinous Cystadenoma.—(64 cases.) In this small group, 30 per cent or 19 instances were found in patients between thirty and forty years of age; fifteen per cent or 23 patients in the third decade and 20 per cent or 13 patients in the forty- to fifty-year decade. Thus 65 per cent of these tumors occur in women between the ages of twenty and fifty years. In young women between the ages of ten and twenty years, there were 7 cases or 12.5 per cent. The oldest patient in whom this tumor was found was sixty-eight years of age, the youngest was fourteen years.

Endometriosis of the Ovary.—(43 cases.) The greater number, namely 72 per cent, of these growths are found in the two decades between twenty and forty years; however, in the combined periods between twenty and fifty years, 93 per cent of all these tumors are found.

Papillary Serous Cystadenomas.—(36 cases.) Sixty per cent or 22 instances in this small group of benign neoplasms are found in patients over 40 years of age. The highest incidence is in the sixth decade, namely, 10 cases or 30 per cent. It

is the only type of benign growth which predominates in patients of advanced age. This is unusual, since only malignant tumors are more common in advanced years. The youngest patient was 11 years of age and the oldest 88 years of age.

Tuboovarian Cysts.—(29 cases.) Although the number of cysts is limited, the age incidence occurs as one would expect, i.e. 40 per cent or 11 cases in women between twenty and thirty years; 10 cysts, or 30 per cent, among thirty- to forty-year-old patients; and the remainder in patients between forty and fifty years. No case occurred in a patient under twenty years of age or over sixty years of age.

Fibromas.—(24 cases.) These tumors are distributed over all decades between ten and seventy years. In the fourth decade 37 per cent were found; in the sixth decade, 20 per cent; and in the third and fifth decades, an incidence for each of 17 per cent was found.

Papillary Pseudomucinous Cystadenocarcinoma.—(11 cases.) This small group of cancers is divided equally among the patients of all decades from twenty to seventy years, and corresponds roughly with the frequency of its benign form.

Embryonal Neoplasms.—(10 cases.) The 80 per cent incidence in young patients between ten and twenty years of age is striking. Six of the teratomas and both the disgerminomas are found in this age group.

Rare Malignant Tumors.—(28 cases.) More than half of the sarcomas and carcinomas are found in patients over forty years of age; namely, 7 of the 9 sarcomas and 10 of the 19 carcinomas; the former are fibrosarcomas, hemangio- and angiosarcomas; the latter are made up of medullary, Krukenberg and solid carcinomas, as well as both the squamous cell carcinomas in dermoid cysts. In patients under twenty years, the sarcomas found were spindle, round cell, and hemangiosarcomas, and the carcinomas were 4 of the 6 Krukenberg tumors.

One carcinoma was found in the ten- to twenty-year age group and one in the sixty- to seventy-year age group. Thus, 70 per cent of the sarcomas and 67 per cent of the carcinomas were in women over forty years of age; 22 per cent of the remaining cancers were in patients between thirty and forty years.

It is obvious that ovarian sarcoma incidence is not in accord with these figures.

SUMMARY

Considering the entire group of 1,101 tumors, it is observed that 58 per cent were removed from women between the ages of twenty and forty years; (31 per cent in the fourth and 27 per cent in the third decades); 30 per cent of the tumors were found in patients over forty years, and 10 per cent under twenty years.

The predominating number of simple cysts (82 per cent), dermoid cysts (83 per cent), pseudomucinous cystadenomas (73 per cent), and endometriosis of the ovary (93 per cent) were found in the age group between twenty and fifty years.

The predominating number of papillary serous (84 per cent), and pseudomucinous cystadenocarcinoma (72 per cent), also papillary cystadenomas (72 per cent) and fibromas (74 per cent) are found in the age group between thirty and sixty years.

Thus, in the period of ovarian activity, namely, between twenty and forty years, more than half the ovarian tumors are found.

IIIB. FREQUENCY OF OVARIAN TUMORS BY AGE GROUPS (DECADES)

The largest number of ovarian tumors is found in women between the ages of thirty and forty years; 347 cases are recorded, an incidence of 31 per cent. Simple cysts comprise 55 per cent of this number, or a total of 189 cases. Dermoid cysts, then papillary serous cystadenocarcinomas, follow in order of their frequency in this decade; namely, 16 per cent and 10 per cent.

Next in frequency is the third decade, twenty to thirty years, in which 302, or 27 per cent, of ovarian tumors were found. The 162 simple cysts representing 53 per cent of these tumors are the most frequent, then, 74 dermoid cysts, constituting 21 per cent, and 15 pseudomucinous cystadenomas, namely, 5 per cent.

Third in order of frequency is the fifth decade, forty to fifty years, in which are 216 ovarian tumors, or 19 per cent of all ovarian newgrowths. Again, simple cysts have the highest frequency, namely, 81 instances or 37 per cent. Fifty-five papillary serous cystadenocarcinomas, namely, 25 per cent, and 24 dermoid cysts, namely 11 per cent, are also noted as second and third in frequency.

The 113 tumors found in the second decade, namely, between ten and twenty years, bring this age group into fourth place in order of its ovarian tumor incidence. The simple cyst (77 cases) is the principal neoplasm in this decade, with an incidence of 68 per cent. The dermoid and pseudomucinous cystadenomas follow in order.

In the sixth decade only 93 ovarian tumors are found, namely 8.3 per cent. This age group is fifth in order. The most frequent tumor is the papillary serous cystadenocarcinoma, constituting 44 per cent or 40 instances. There was a twelve per cent incidence of papillary serous cystadenoma, namely 11 cases, and an 11 per cent incidence of simple cysts, namely, 10 cases.

Between the ages of sixty and seventy years, there were 26 cases constituting only 2.3 per cent of all ovarian tumors; forty per cent of these are represented by the 10 papillary serous cystadenocarcinomas, 20 per cent by 5 dermoid cysts and 8 per cent by 2 simple cysts.

SUMMARY

It is of interest to note that of the 786 tumors in patients between ten and fifty years, 509 or 65 per cent were simple cysts. The second outstanding tumor, the dermoid cyst, has a 21 per cent incidence (166 cases), the papillary serous cancer with 11 per cent incidence (89 cases) and the papillary pseudomucinous cancer with a 3 per cent incidence (22 cases), are third and fourth in frequency.

In 115 patients under twenty years, simple cysts predominate; there were 77 (or 67 per cent) of these. Dermoid cysts are second in frequency with an 11 per cent incidence (15 tumors).

One hundred and twenty-one or 11 per cent of all ovarian tumors are in women over fifty years; papillary serous cystadenocarcinomas comprise forty per cent (50 cases) of this group. Its benign form is second in incidence, namely 11 per cent (13 cases). Twelve simple cysts were 10 per cent of this entire age group.

IIIC. MALIGNANT AND BENIGN TUMOR INCIDENCE IN THE ENTIRE GROUP, IN MENOPAUSE AND PREMENOPAUSE

There are 139 patients found in menopause, and 963 in the premenopause age. Eighty or 58 per cent of the former and 11.5 per cent of the latter had ovarian malignancies. Thus, a climacteric patient with an ovarian mass has a 58 per cent possibility of ovarian cancer. Eighty or 42 per cent of the 191 ovarian carcinomas in this series occurred in menopause women, and 111 or 58 per cent in premenopause women.

Fifty-eight or 6.3 per cent of the 910 benign tumors were found in menopause women and 93.7 per cent or 852 patients were in the premenopausal group.

TABLE III

	MENOPAUSE		PREMENOPAUSE		TOTAL	
All tumors	138		963		1,101	
Malignant	80	58%	111	11.5%	191	17%
Benign	58	42%	852	88.5%	910	83%

IIID. MALIGNANCY DURING MENOPAUSE

Sixty-two or 71 per cent of the 80 cancers removed from patients in menopause were papillary serous cystadenocarcinomas. This number comprises 43 per cent of all (152) these serous cancers.

Both squamous cell carcinomas in dermoid cysts, the single angiosarcoma and the carcinoma of undetermined type occurred in menopause patients. In this group also are found 75 per cent of fibrosarcomas, 67 per cent of solid carcinomas, 50 per cent of 6 medullary cancers and 2 hemangiosarcomas. Four of the 11 pseudomucinous cystadenocarcinomas were operated during climacterium. Only 1 of the 6 colloid cancers was removed from a menopause patient.

Spindle cell, round cell and carcinosarcoma were not found among menopause patients.

IIIE. BENIGN TUMORS DURING MENOPAUSE

Only 6.4 per cent or 58 of the 910 benign growths were found in menopause patients. The following make up this number: 36 per cent of the 36 papillary serous cystadenomas, namely, 13 cases; eight per cent of the 64 papillary pseudomucinous cystadenomas, or 5 cases; and 7 per cent of the 182 dermoid cyst patients, namely, 13 cases. Between 2 and 3 per cent of each of the following tumors were removed from climacteric women: simple cysts, endometriosis of the ovary, and fibromas. No case of tuboovarian cyst, teratoma or disgerminoma was observed in a menopause patient.

IV. MARITAL STATUS, PARITY AND GRAVIDITIES AMONG OVARIAN TUMOR PATIENTS

Seventy-five per cent of all ovarian tumors are found in married patients and 25 per cent in single women. (670 were married and 240 were single.)

A. *Benign and Malignant Tumors in Relation to Marital Status.*—In married women are found 75 per cent (682) of the 910 benign tumors, and 81 per cent (155) of the 191 malignant tumors.

B. *Relation of Marital Status to Benign and Malignant Tumors.*—Benign tumors are found in 87 per cent (240) of the 276 single patients and 81 per cent (668) of 825 married women. Malignant tumors make up the remainder. Moench reports that 76 per cent to 89 per cent of serous benign and malignant tumors and solid cancers occur in married women.

C. *The Nature of the Tumor in Relation to Parity.*—Although 825 patients in the group were married only 355 or 43 per cent were parous. Thirty per cent of 190 malignant tumors and 32 per cent of 911 benign tumors were in parous patients, while 70 per cent of 190 malignant tumors and 68 per cent of 911 benign tumors were in nonparous women. Thus both types are twice as common in nonparous women.

D. *Parity in Relation to the Nature of the Tumor.*—Sixteen per cent of both parous and nonparous patients had ovarian cancer, while 84 per cent of each had benign tumors of the ovary. Thus, both parity and nonparity are five times more common among benign than among malignant neoplasms.

E. *Gravidities Among Ovarian Tumor Patients.*—Parity among the 825 married women is 43 per cent; among all patients regardless of marital status, 32 per cent. Among patients with dermoid cysts, simple cysts, and papillary serous cystadenocarcinomas, parity is from 28 per cent to 36 per cent. In the small groups, with the exception of fibrosarcomas, parity is from 20 per cent to 53 per cent. All disgerminomas, spindle cell sarcomas, round cell, angio- and hemangiosarcomas, as well as carcinosarcomas, occurred in nulliparous women of or past the childbearing age. Three of the 4 fibrosarcoma patients had borne children. One

child gravidity is most common: 29 per cent of parous women had one child and 25 per cent had two children. In a tuboovarian cyst patient, 20 pregnancies were reported. Moench reports between fifty per cent and 63 per cent parity in benign and malignant serous tumor patients and solid carcinomas. My figures are 40 per cent less than these. Randazzo states that 32 per cent of ovarian cyst patients are sterile.

V. UTERINE BLEEDING

Since ovarian structure in most instances in this group had undergone considerable, if not complete alteration, the high incidence of normal menses, namely, 54.3 per cent or 598 cases among 1,101 ovarian tumors is significant, especially in the light of the present facts with regard to the relationship of the ovary to the menstrual function.

Hyperfunctional ovarian bleeding occurred in 292 patients, or 26.5 per cent of all tumor cases. There were 123 of these or 11 per cent with metrorrhagia, 136 or 12.3 per cent had menorrhagia, and 3.3 per cent or 33 patients had menometrorrhagia.

Hypofunctional ovarian bleeding incidence is 17.9 per cent, representing 198 patients. Of these, 138 patients or 12.3 per cent were in the menopause. Three per cent or 38 patients complained of secondary amenorrhea, and 2 per cent or 22 patients complained of oligomenorrhea. Neither of the latter two groups can be considered climacteric in orgin since these patients were all young women.

Normal Menses.—Those tumor groups showing highest incidence of normal bleeding, namely, 64 per cent in each, are the dermoid cyst and the pseudomucinous cystadenocarcinoma. Next in order is the 60 per cent incidence of a normal cycle among patients with pseudomucinous cystadenomas. Fifty-six per cent of both simple cyst patients and women with ovarian endometriosis reported normal bleeding.

The tuboovarian cyst and papillary serous cystadenocarcinoma patients show 45 per cent incidence of regular uterine bleeding, and among the papillary serous cystadenoma patients the incidence was 41 per cent.

Three of the 8 teratomas, 2 of the 6 medullary carcinomas, and one of the 6 colloid cancers, as well as one of the 4 fibrosarcoma patients, reported normal uterine bleeding.

Twenty-five per cent of 24 fibroma patients had normal bleeding. In the single instances of the following tumors there were also normal menses; namely, spindle cell sarcoma, carcinosarcoma, and solid carcinoma.

Menorrhagia.—This form of bleeding is not observed with great frequency. It appears most frequently among ovarian endometriosis cases, namely, thirty per cent incidence, among 20 per cent of the tuboovarian cysts, and in 16 per cent of the simple cyst patients.

Dermoid cysts and both benign and malignant papillary serous tumors, papillary pseudomucinous adenomas and teratomas, each show a small number of instances of menorrhagia. In a patient with purpura-hemorrhagica, menorrhagia was also noted.

Except for one round cell sarcoma patient, there is not a single instance of this type of bleeding among the rare malignancies or the embryonal tumors.

Metrorrhagia.—The highest incidence of this form of bleeding, namely 34 per cent, was found among the tuboovarian cyst patients; 14 per cent of simple cysts and nine per cent of patients with endometriosis of the ovary show this form of uterine bleeding.

It occurred in 33 per cent of the fibroma cases, in 5.2 per cent of serous papillary cancer, and in 7.7 per cent of pseudomucinous papillary cystadenoma patients.

Ten per cent of the dermoid cyst patients complained of this symptom. Among colloid (Krukenberg) and medullary cancers only a few instances are reported.

Menometrorrhagia.—This is an uncommon form of bleeding in patients with ovarian growths. Its presence is noted in only four of the groups.

Simple cyst patients show an incidence of 5.3 per cent and dermoid cysts, serous papillary cystadenocarcinomas and pseudomucinous papillary cystadenoma patients complained in about 1.5 per cent of the instances in each group.

Menopause.—One hundred and thirty-eight or 12.5 per cent of all ovarian tumors were removed from patients during menopause. Forty-two per cent or 58 of the above number of patients were operated upon for benign tumors. The incidence of menopause among the types of benign tumors is as follows: Thirty-six per cent of serous papillary cystadenomas and 21 per cent of fibromas were found in climacteric women. Only 2.5 per cent, respectively, of simple cysts and ovarian endometriosis occurred during this period. Eight per cent of both dermoid cysts and pseudomucinous papillary cystadenomas were removed from menopausal women.

Fifty-eight per cent or 80 of the 138 menopausal tumors were cancerous. Their distribution is as follows: Sixty-two or 41 per cent of the 152 serous, and 4 or 36 per cent of the 11 pseudomucinous papillary cyst adenocarcinomas were operated upon during menopause. Three of the 6 medullary cancers, 2 of the solid cancers and both of the squamous cell cancers developed in dermoid cysts were removed from patients of menopause age.

All three fibrosarcomas were in menopause patients.

Angio- and hemangiosarcoma as well as colloid cancer, in one instance each, fall in this group also.

Menopausal Uterine Bleeding.—This type of bleeding occurs only 14 times in 1,101 tumor patients, an incidence of 1.3 per cent. Two of the 522 simple cyst patients, namely, 0.4 per cent; 6 of the 152 papillary serous carcinomas, namely, 4 per cent; and 2 of the 4 fibrosarcoma patients, namely, 50 per cent, are in this group. This condition is also noted in one of the colloid cancer patients, as well as in a case of ovarian fibroma and in a patient with medullary carcinoma of the ovary.

Amenorrhea.—Thirty-eight patients of menstruating age had amenorrhea, an incidence of 3 per cent. 12.8 per cent of the pseudomucinous papillary adenomas (8 of 64 cases), 5 per cent of the dermoid cyst patients (9 of 182 women), and 3 per cent of the simple cyst cases (15 of 522 patients), had amenorrhea.

Other Menstrual Irregularities.—Other forms of abnormal bleeding do not appear frequently enough to warrant more than passing mention. In one of the patients with teratoma of the ovary, purpura hemorrhagica was noted with menorrhagia.

Primary amenorrhea occurred in two of the young patients with teratoma and also in a sixteen-year-old girl with bilateral fibromas of the ovary. Clinically, in the latter case, a mannish voice and stature, and hypertricosis were observed. The tumors were grapefruit and lemon size, respectively, and had undergone calcific and fatty degeneration.

Oligomenorrhea, interval staining, spotting as in ectopic pregnancy, and prepuberty bleeding occurred uncommonly and without particular frequency in any tumor type. Four instances of the latter type of bleeding (prepuberty bleeding) among young patients with dermoid cysts are of interest.

The wide variety of vaginal bleeding coincidentally found with 1101 ovarian tumors indicates that the diagnostic importance of this symptom cannot be stressed. The preponderance of the normal menses over all other bleeding forms, in spite of the partial or complete anatomical ovarian change, is striking.

It may be concluded that structural ovarian change appears to have no relation to the functional activity of the ovary.

VI. DYSMENORRHEA

There were 131 instances of this symptom among 858 cases; the latter figure excludes patients amenorrheic because of menopause, oligomenorrhea and other causes. The average total incidence of this symptom is 15 per cent. (Table IV.)

Dysmenorrhea is found with endometriosis of the ovary in 21 per cent of 42 patients. Simple cysts show 19 per cent incidence and papillary serous and pseudomucinous cystadenomas show a 12 per cent and 13 per cent frequency, respectively, whereas 14 per cent is observed in malignant pseudomucinous cystadenocarcinomas.

TABLE IV. DYSMENORRHEA

TYPE	NO. OF PATIENTS	DYSMEN-ORRHEA	PER CENT OF TOTAL
Simple cysts	478	94	19.4
Dermoid cysts	156	15	9.5
Papillary serous cystadenocarcinoma	82	3	3.6
Papillary pseudomucinous cystadenoma	19	6	12.0
Endometriosis of the ovary	42	9	21.0
Papillary serous cystadenoma	22	3	13.0
Papillary pseudomucinous cystadenocarcinoma	7	1	14.0
Tuboovarian cysts	29	0	0
Fibroma	23	0	0
Total	858	131	15.0

VII. METASTASES IN MALIGNANT OVARIAN TUMORS (TABLE V)

At operation 76 per cent of 190 patients with ovarian malignancy were found to already have metastases; 412 separate foci were noted. In many patients there were numerous sites of spread. Metastases was not found with round cell and angiosarcoma.

A. *Incidence by Body System.*—The greatest number of areas of metastases was found in the *gastrointestinal* tract and *peritoneum,* namely, 105 in each, or 26 per cent of all foci of spread.

There are 79 instances of gastrointestinal tract invasion from 152 papillary serous cancer, 14 instances by 6 colloid or Krukenberg tumors, 5 instances by 6 medullary carcinomas, and 4 instances by 11 papillary pseudomucinous cystadeno-carcinomas. Among 2 squamous cell carcinomas in dermoid cysts the intestinal tract was involved once, and in the 2 hemangiosarcomas, 2 intestinal foci of spread were found.

Eighty-seven instances or 57 per cent of peritoneal invasion were noted in the 152 papillary serous cystadenocarcinomas, 5 instances or 45 per cent among the

TABLE V. INCIDENCE OF THE METASTATIC FOCI IN 190 OVARIAN CANCERS

SITE	NUMBER	
Peritoneum	106	26%
Gastrointestinal tract	105	26%
Gynecologic system	66	16%
Omentum	47	11%
Other organs	34	9%
Lymphatic tract	23	5%
Genitourinary tract	18	4%
Respiratory tract	13	3%
Total number of metastatic foci	412	

11 papillary pseudomucinous cystadenocarcinomas, and 4 peritoneal metastases each were noted in both colloid and medullary cancers. Carcinosarcoma, solid carcinoma and squamous cell carcinoma in a dermoid cyst each account for one instance of peritoneal spread, while in both hemangiosarcoma patients the peritoneum was also involved.

The gynecological tract contains 66 of the 412 foci or 16 per cent: The tumor accounting for 57 of the 66 instances is the papillary serous cystadenocarcinoma. The most frequent structure involved is the uterus; next in frequency are the homolateral tube and contralateral ovary. The contralateral tube and broad ligaments contain metastases of slightly less frequency.

The pseudomucinous cystadenocarcinoma accounts for 2 uterine foci. The colloid cancers show spread to the tube and broad ligament and infundibulo pelvic ligament, and the medullary cancer shows spread to the broad ligament in 3 instances and also to an inguinal hernia sac.

Other involved structures are mesosalpinx, ovarian cortex, rectovaginal septum, vaginal wall and fornix, cervical stump and parametrium.

The omentum revealed 47 foci or 11 per cent of all sites of spread. Thirty-five of the 47 instances of omental involvement were papillary serous cyst adenocarcinoma. There were 3 instances each among papillary pseudomucinous cyst adenocarcinomas and colloid cancer, and 4 among 6 medullary carcinomas. In one of the squamous cell carcinomas in dermoid cyst and in one hemangiosarcoma patient, the omentum was also involved with metastasis.

Various organs reveal 34 carcinomatous metastases, an incidence of 9 per cent, 15 of the 20 liver metastases, 4 abdominal wall foci and malignant spread to breast, adrenal, spleen and subcutaneum originated from papillary serous cystadenocarcinomas. The liver was involved also by pseudomucinous carcinoma, spindle cell and hemangiosarcoma. Colloid and medullary cancers showed spread to the umbilicus and also to the spleen and an abdominal scar.

Although malignancy spreads through the *lymphatic stream*, only 23 instances of cancer were found, an incidence of 5 per cent. The iliac, abdominal, periportal, mediastinal, aortic, perirenal, axillary and gastric lymphatics were invaded in all instances from the papillary serous cystadenocarcinomas. Four of the 13 metastatic pelvic node cancers arose from the pseudomucinous and 7 from the serous papillary cystadenocarcinomas. Two pelvic node metastases took origin from the squamous cell carcinomas in dermoid cysts.

The genitourinary tract contained 18 cancerous foci, or 4 per cent of the total number: The bladder was involved 9 times in all; six times from serous papillary malignancies, one from a colloid, and one from a medullary carcinoma. An angiosarcoma was the origin of another.

Patients with squamous cell carcinoma in a dermoid cyst, medullary carcinoma, and papillary serous cystadenocarcinoma had both unilateral and bilateral ureteral metastases.

There was one case of pyonephrosis in a serous ovarian cancer. Ureteral orifices were involved twice by papillary serous cystadenocarcinoma and in a third patient with this tumor the vesicocervical junction was completely invaded.

The respiratory tract accounts for 13 cancerous foci or 3 per cent. Papillary serous cystadenocarcinomas were the origin of metastases to the right lung in 5 cases and to the pleura and diaphragm in 4 instances each. Pleural effusion was noted in 5 patients, each of whom had papillary serous cystadenocarcinoma of the ovary. The incidence of this finding is 2.7 per cent in the 190 patients. The respiratory tract accounts for 3.1 per cent of all metastatic foci from ovarian cancer.

B. *Incidence in Single Structures.*—Of the single structures involved by metastases, pelvic peritoneum has the highest incidence, namely, 73 instances or 17 per cent. The omentum, discussed above, is second; culdesac was involved separately in 13

patients. The small intestines (30) and sigmoid (27) contained 7.2 per cent and 6.5 per cent of metastatic foci, respectively; 5.8 per cent or 24 instances of rectal metastases were observed. Liver and abdominal peritoneum were invaded 20 times each, or 4.8 per cent. In 15 instances, uterine spread was noted, and 10 foci in retroperitoneal nodes were found.

Abdominal carcinomatoses and "frozen" carcinomatous pelvis were observed in 12 patients, respectively. Structures involved also were stomach, duodenum, bladder, ureter, and lung, pleura and diaphragm. The vagina, cervical stump, rectovaginal septum as well as spleen, adrenals, breast, pericardium and mesentery, were sites of metastasis from ovarian cancer. Nodules were demonstrable also in the umbilicus, in abdominal scars and in an inguinal hernia sac.

Retroperitoneal pelvic lymphatics were invaded in 13 instances; iliac and abdominal groups in two patients. Involvement of the periportal, mediastinal, aortic, perirenal axillary and gastric nodes is evidence of the invasive character of carcinomas of the ovary.

C. *Metastasis in Each Cancer Group.*—One hundred forty-four of the 190 malignant tumors were found, upon laparotomy, to have invaded either surrounding or distant body structures. This high incidence of 76 per cent is an indication that symptoms are either very mild or occur too late in the disease for a reasonable possibility of operative cure. Many patients present themselves in a stage of carcinomatosis peritonei, with symptoms of but two to three months duration!

Seventy-seven per cent of the 152 serous, and 73 per cent of the 11 pseudomucinous papillary cystadenocarcinoma tumors had already invaded secondary structures before surgical treatment could be employed.

All of the 6 Krukenberg cancers, and 83 per cent of the 6 medullary tumors had spread before these patients were treated surgically.

Both hemangiosarcomas and the single cases of spindle cell and carcinosarcoma had metastatic foci when laparotomy was performed.

The fibrosarcoma, the solid sarcoma, and the squamous cell carcinoma in a dermoid cyst had metastasized in 25 to 50 per cent of the patients.

The single angio- and round-cell sarcoma showed no metastasis.

D. *Ascites in 190 Ovarian Malignancies.*—Fifty-four per cent (or 103) of malignancies were found with intraabdominal or pelvic fluid. (Lippert's incidence for ascites is 78 per cent and Moench reports 79 instances in 274 ovarian malignancies or 32 per cent.)

Clear, bloody, or purulent fluid was common to all malignant tumors. Seventy-one per cent of instances with ascites had clear fluid, 22 per cent, bloody, and 7 per cent purulent fluid.

Ninety-five per cent of ascites was due to papillary serous cystadenocarcinoma, which predominates also in all the above types of ascitic fluid.

Of 152 papillary serous carcinomas, 95 or 62 per cent had ascites; of the 11 pseudomucinous cancers, 3 or 27 per cent, and of the 12 medullary and colloid tumors, 4 or 33 per cent, had ascites; one of the 4 fibroma cases had free fluid. (Zangmeister reports ascites in 29 of 36 fibromas [Kaufmann Path. p. 1581, v. 2] and Pfannenstiel a 25 per cent incidence for ascites for these growths.)

VIII. SYMPTOMS AND SIGNS IN PATIENTS WITH OVARIAN TUMORS

A total of 1814 symptoms was noted in the histories of all patients (1101) with ovarian tumors, among which are 900 benign and 163 malignant growths. Symptoms are classified as pain, gastrointestinal, abdominal, bladder, respiratory, and miscellaneous. A comparison between symptoms due to benign and malignant tumors is made.

Most complaints were mild in character and their insidious onset accounts for late recognition of disease. Symptomatology was not always referable to the pelvis and therefore many patients reached the gynecologist late in the course of disease.

Pain.—Pain constitutes 44 per cent of all symptoms; 75 per cent of all the patients, namely 802, had pain; 11 per cent of this symptom is found among 91 malignant, and 89 per cent among 711 patients with benign tumors. It may also be noted that 91, or 55 per cent, of all malignant and 711, or 79 per cent of all benign tumor patients complained of pain. Pain is slightly more frequent in benign growths.

Seventy-five per cent of simple cysts, 95 per cent of dermoid cysts, and 65 per cent of papillary pseudomucinous cystadenomas produced pain. Ninety-three per cent of patients with endometriosis of the ovary, 75 per cent of papillary serous cyst-adenoma patients, 76 per cent of tuboovarian cyst patients, and 58 per cent of fibromas also suffered from pain. Fifty-six per cent of papillary serous and 45 per cent of papillary pseudomucinous cancer patients complained of pain. (Moench states that 52.6 per cent of 274 patients had pain.)

Thus, pain is a fairly constant feature, but it is either so mild in its nature or so delayed in its onset that its importance in early diagnosis is greatly diminished.

Gastrointestinal Symptoms.—There are 358 or 19 per cent of 1814 symptoms in this group. Seventy-four instances or 20 per cent of these complaints are found in malignancy patients and 284 or 80 per cent in the benign growth patients. There are 74 symptoms among the 163 malignancy cases, a 45 per cent incidence. The 900 benign tumors show an incidence of 27 per cent. Thus, these symptoms occur one and a half times more frequently in patients with malignant tumors.

Vomiting and nausea are the principal complaints, representing 33 per cent and 26 per cent, respectively, of all intestinal symptoms. Thirteen per cent of these instances occurred in malignant tumor patients. Constipation, cramps, and dyspepsia are frequent symptoms. Four and four-tenths per cent of all intestinal symptoms are caused by bowel obstruction and 88 per cent of these were in malignant patients. Rectal complaints, few in number, were manifest only in carcinoma patients.

Abdominal Signs.—Two hundred ninety-five, or 16 per cent of the 1814 complaints comprise this group; 28 per cent of these were in malignancy patients; 235 instances of abdominal mass represent 80 per cent of these complaints; 35 per cent of patients with abdominal mass had ovarian cancer. Abdominal rigidity (17 per cent of this group) was found in 50 patients with simple cysts.

Bladder Symptoms.—One hundred thirty-eight symptoms represent only 8 per cent of all the complaints. Malignancy patients account for 32 per cent of bladder symptoms. Dysuria, urinary frequency, and urgency occur in this order of incidence. Dysuria comprises over 50 per cent of bladder symptoms.

TABLE VI. SUMMATION OF SYMPTOMS AND SIGNS IN BENIGN AND MALIGNANT TUMORS

SYMPTOMS	MALIGNANT TUMOR PATIENTS 163	PER CENT	BENIGN TUMOR PATIENTS 900	PER CENT	TOTAL NO. 1,063
Pain	91	11	711	89	802
Gastrointestinal	74	20	284	80	358
Abdominal signs	85	28	210	72	295
Bladder symptoms	44	32	94	68	138
Respiratory symptoms	4	57	3	43	7
General symptoms	79	36	135	64	214
	377	20	1,437	80	1,814

Respiratory Symptoms.—Cough, dyspnea, and hemoptysis are complaints infrequently heard. They are noted only among carcinoma patients. Pleural effusion was demonstrated in a case of pseudomucinous cystadenocarcinoma.

General Symptoms and Signs.—Fainting, vertigo, shock, headache, and nervousness comprise 18 per cent of this group. Chills and fever are infrequently noted. Twenty-eight sterility complaints were found in simple and dermoid cyst patients. Hypertrichosis and mannish voice were found in a patient with fibroma of the ovary.

IX. SITE OF PAIN AND POSITION OF OVARIAN TUMORS

(a) *Sites of Pain* (802 cases): This symptom occurred in 75 per cent or 802 of all the patients. In the remaining 25 per cent, pain was either not mentioned or not recorded. A fair concept of the correlation between the sites of pain and pathology is obtained by comparing the percentage incidence of each.

Pain in the right, left or bilateral lower quadrants is a complaint in 70 per cent of these women; the remaining 30 per cent is made up of various other body areas, not directly referable to the pelvis.

Twenty-seven per cent and 25 per cent of the complaints, respectively, were referable to the right and left lower quadrants, while 18 per cent were bilateral. Thus, unilateral is about three times more frequent than bilateral pain. Back and abdominal complaints are not infrequent. Suprapubic, epigastric and thigh pains occur often, while right upper quadrant, umbilical and left shoulder pains are rare.

(b) *Position of All Tumors* (1,063 cases): In this series, 21 per cent of all ovarian tumors were bilateral.

My figures of right (44 per cent) and left side (35 per cent) incidence are similar to those of other authors. The right side incidence is slightly greater. One per cent of ovarian tumors in this series is intraligamentous.

Position of Malignant and Benign Tumors.—Bilaterality occurs in 55 per cent of all malignancies. The incidence of bilaterality among sarcomas is 10 per cent. Papillary serous cystadenocarcinomas show 57 per cent bilaterality. Solid carcinomas are found bilateral in 10 per cent in this series.

Among the *benign tumors,* simple cysts are bilateral in 15 per cent of instances. Dermoid cysts are bilateral in 11 per cent of cases. Papillary serous cystadenomas are found bilaterally in this series in 22 per cent, by Frank-Feresten in 12.7 per cent, and by Pfannensteil in 60 per cent of cases. Six per cent of papillary pseudomucinous cystadenomas are bilateral. Fibromas appear bilateral in 15 per cent of cases: in the Frank-Feresten series, 29.4 per cent is reported and Hoon reports 3.6 per cent.

SUMMARY

From the total figures in table VII, it is noted that (a) unilateral pain is three times more frequent than bilateral pain, while the unilateral tumor is four times more frequent than the bilateral; that (b) only 27 per cent of the sites of pain were

TABLE VII. CORRELATION BETWEEN THE PAIN SITE AND THE SITE OF THE PATHOLOGY IN 802 PATIENTS

	R.L.Q.	L.L.Q.	BILATERAL	BACK, ABDOMEN, SHOULDER, R.U.Q., THIGH, ETC.
Pain location in 802 cases	27%	25%	18%	29%
Tumor location in 1,063 cases	44%	35%	21%	0
Per cent incidence of correlation between pain and pathology site	61%	70%	86%	0

in the right lower quadrant and 44 per cent of the tumors were on that side; that (c) only 25 per cent of pain sites were in the left lower quadrant, while 35 per cent of the tumors were on that side; that (d) 18 per cent of pain area was bilateral and here the pathology was bilateral in 21 per cent of cases.

Thus, 61 per cent of the right side and 70 per cent of left side tumors cause homolateral pain, while 80 per cent of bilateral tumors are accompanied by bilateral pelvic pain.

The greatest coincidence of pain sites and pathology is noted among bilateral ovarian tumors.

X. SEDIMENTATION TEST

This test was performed 298 times for the 1101 patients or 27 per cent of all cases. The recent clinical use of the test accounts for the small number of instances presented. There were 71 patients with rapid sinking time indicating infection; 60 per cent or 180 showed a rate between thirty and sixty minutes, and the remainder 16 per cent or 47 patients showed a response over 60 minutes and as prolonged as 340 minutes.

The significance of sedimentation rate is of importance in inflammatory adnexal conditions, in degenerations of benign and malignant tumors, and in infections superimposed upon twisted or infarcted ovarian tumors.

Sixty per cent of simple cyst patients showed a sedimentation rate between thirty and sixty minutes and 14 per cent less than thirty minutes; twenty-five per cent of them were over one hour. Sixty per cent of the cases in which papillary serous cyst adenocarcinoma was found had sedimentation rates under thirty minutes; 41 per cent were between thirty and sixty minutes. Fourteen per cent of patients with dermoid cysts had rapid sedimentation rates; 66 per cent were over thirty minutes and 12 per cent were over sixty minutes.

Sixty per cent of tuboovarian cyst patients had a sedimentation rate between thirty and sixty minutes; 40 per cent were under thirty minutes. However, only 3 per cent of this small group of tumor cases, namely, 10 patients, were tested.

CONCLUSIONS

1. A single complete analysis of clinical and pathologic data from a large number of ovarian tumor operations is warranted, since no such report appears in the literature. The facts, of interest to the surgeon and clinician, justify publication.

2. *Frequency:* The simple and dermoid cysts are first and second in order of incidence. Papillary serous cancer occupies a position of hitherto unreported high frequency, namely third; it constitutes 80 per cent of all ovarian cancers, and is 4 times more frequent than its benign form. It is 14 times more frequent than the pseudomucinous cancer of the ovary.

3. *Malignancy Incidence:* 17.3 per cent of all ovarian tumors are malignant; 95 per cent of these are cancer and 5 per cent sarcoma.

4. *Age Incidence:* 58 per cent of all ovarian tumors are in patients between twenty and forty years; 30 per cent are over forty years and 12 per cent under twenty years.

Sixty-seven per cent of cancer and 70 per cent of sarcoma were in women over forty years; 22 per cent of cancer was in patients between twenty and thirty years. Sixty per cent of benign serous tumors are in patients over forty years.

The fourth decade contains 31 per cent of ovarian tumors, the third decade 27 per cent and the fifth decade, 19 per cent. Simple cysts predominate in all three decades.

5. *Marital Status and Parity:* 75 per cent of tumors of the ovary are found in married patients; 81 per cent are benign and 19 per cent malignant; 43 per cent of married women with ovarian growths were parous; 30 per cent of malignant tumors were in parous women.

6. *Menses:* Normal menses occur in 54.3 per cent of patients with ovarian tumors; hyperfunctional bleeding in 26.5 per cent and hypofunctional bleeding in 17.9 per cent.

In view of the present knowledge with regard to the ovarian effect on menstruation, the high incidence of normal menses is notable.

Eleven per cent metrorrhagia, 12.3 per cent menorrhagia, and 3.3 per cent menometrorrhagia; and 12.3 per cent menopause, 3 per cent secondary amenorrhea, and 2 per cent oligomenorrhea, are the figures obtained.

In 58 per cent of menopause patients malignancies were found. Thus a climacteric patient with an ovarian tumor has a 58 per cent possibility for cancer. Eighty per cent of all malignancy occurs in menopause women.

7. *Dysmenorrhea:* The incidence of this symptom was only 15 per cent.

8. *Metastases* are noted at operation in. 76 per cent of ovarian cancer patients; 80 per cent of these are due to papillary serous cystadenocarcinoma. The insidious character of an ovarian malignancy is indicated by this figure, as well as the difficulty in an early diagnosis.

Twenty-six per cent of metastases are found in the gastrointestinal and peritoneal systems. The gynecologic tract and omentum contain 16 per cent and 11 per cent, respectively. Lymphatics, genitourinary and respiratory systems, and various organs are found to have the remainder of foci.

Ascites incidence is 54 per cent in malignancy; 95 per cent of this finding is caused by papillary serous cystadenocarcinoma; 71 per cent have clear fluid, 22 per cent bloody, and 7 per cent purulent fluid.

9. *Symptoms:* Pain constitutes 44 per cent of all symptoms; 75 per cent of ovarian tumor patients have this complaint. It is not usually severe even in the late stages of carcinoma of the ovary, and is 25 per cent more frequent among the benign tumor cases.

Gastrointestinal symptoms, principally nausea and vomiting, constitute only 19 per cent of complaints; 80 per cent of these occur among the benign tumor patients; 88 per cent of intestinal obstruction is produced by cancer.

Sixteen per cent of all symptoms and signs, totaling 1814, are represented by abdominal manifestations; 72 per cent are in benign tumors. Twenty-one per cent of patients had an abdominal mass, 35 per cent of which was attributed to cancer.

Respiratory symptoms are due only to the cancer metastases, and bladder complaints are caused by benign tumors in 68 per cent of instances.

Eighty per cent of all signs and symptoms are due to benign tumors.

10. *Site of Pain and Tumors:* Seventy per cent of pain was in either the right, left, or bilateral lower quadrants; 18 per cent was bilateral, the remainder was divided equally among the right and left lower quadrants. Twenty-one per cent of tumors are bilateral, 44 per cent right and 35 per cent left; 55 per cent of malignant tumors are bilateral.

Thus, 61 per cent of right side and 70 per cent of left side tumors cause homolateral pain, while 80 per cent of bilateral tumors cause bilateral pain.

11. *Sedimentation Time:* The significance of this test is stressed in inflammatory, degenerative, and infective processes.

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2 EAST EIGHTY-FIFTH STREET

MENSTRUAL BLEEDING AFTER CORPUS LUTEUM EXCISION, FOLLOWED BY ESTRIN OR PROGESTIN THERAPY*

REPORT OF 13 CASES

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THE relative rôles of estrin and progestin in experimental menstrual bleeding monkeys were reported previously (Smith and Engle, 1932, Engle, Smith, and Shelesnyak 1935). These observations were confirmed and additional data added by Corner (1935) and Hisaw (1935).

During this period Kaufmann (1932, 1934) and others demonstrated that not only the proliferative phase of the endometrium could be produced in ovariectomized women by estrin, but also the secretory phase by estrin followed by progestin.

In the experiments on monkeys, it was shown that the uterine bleeding which follows cessation of estrin treatment could be inhibited by

progestin administration, the bleeding being held in abeyance for the duration of the progestin treatment. When progestin treatment was stopped menstruation began in five or six days. After a secretory or progravid endometrium was developed by the use of progestin, the institution of estrin injections did not postpone or prevent the expected
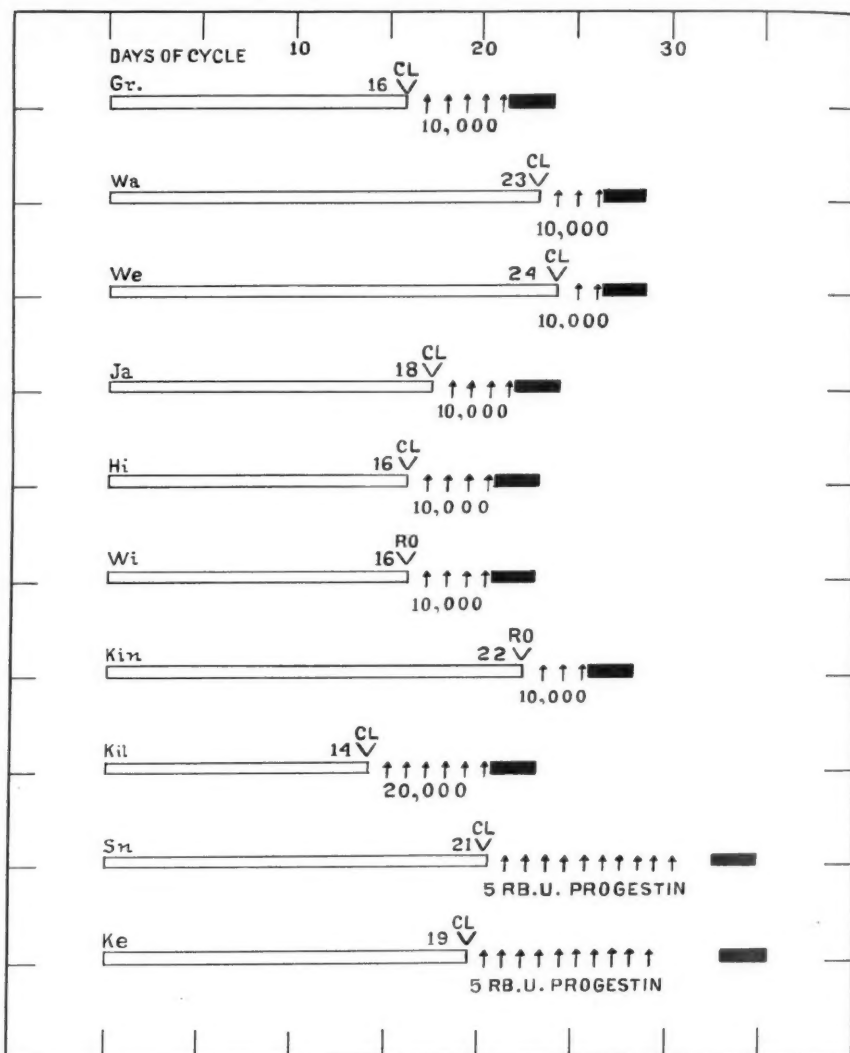
Fig. 1.—Graphic representations of uterine bleeding after corpus luteum ablation, followed by estrin or progestin treatment.

bleeding following progestin withdrawal. Estrin thus has no power to check an experimental menstrual period in the monkey in the presence of a progravid endometrium.

The present report extends these observations to women, and supplies additional evidence as to the rôle of the human corpus luteum in

TABLE I

NUMBER OF CASES	NAME	DIAGNOSIS	TYPE OF PERIOD	TYPE OF OPERATION	TIME AFTER ONSET OF L.M.P.	STARTED TO BLEED AFTER EXCISION OF CORPUS LUTEUM	ESTRIN DAILY R.U.	TOTAL AMOUNT R.U.
1	Gr	Fibroids	28 × 2	Excision of fibroids	16 days	Day 5	10,000	50,000
2	Wa	Fibroids	28 × 3	Excision of one fibroid	23 days	Day 3	10,000	30,000
3	We	Retroversion	28 × 4 – 5	Suspension	24 days	Day 2	10,000	20,000
4	Ja	Myoma uteri	28 × 5 – 6	Myomectomy	18 days	Day 4	10,000	40,000
5	Hi	Retroversion	28 × 3 – 4	Suspension	16 days	Day 5	10,000	50,000
6	Wi	Salpingo-oophorectomy	28 × 7	Right ovariectomy	16 days	Day 4	10,000	40,000
7	Ki	Salpingo-oophorectomy	28 × 8 – 9	Right ovariectomy	22 days	Day 3	10,000	30,000
8	Kil	Retroversion	28 × 5	Suspension	14 days	Day 6	20,000	120,000
							Progestin daily	
9	Pa	Left ovarian cyst	28 × 4	Ovariectomy	28 days	Day 2	2 c.c. = ½ Rb. U.	1 Rb. U.
10	Te	Fibromyoma	28 × 5 – 7	Myomectomy	21 days	Day 4	2 c.c. = ½ Rb. U.	2 Rb. U.
11	Wa	Prolapse of uterus, postpartum	28 × 6	Hysteropexy	20 days	Day 3	2 c.c. = ½ Rb. U.	1¼ Rb. U.
12	Sn	Cystocele-rectocele. Retroflexio uteri	31 × 3 – 5	Pelvic floor repair— suspension	21 days	Day 12	5 c.c. = 5 Rb. U.	50 Rb. U.
13	Ke	Cystocele-rectocele. Retroflexio uteri	26 × 4	Pelvic floor repair— suspension	19 days	Day 14	5 c.c. = 5 Rb. U.	50 Rb. U.

the menstrual cycle. The patients were carefully selected from hospital admissions. An attempt was made to take patients who reported fairly regular cycles. Although it is recognized that the "regular twenty-eight-day" cycle is more of a tradition than a reality, in the absence of more exact data the cases are so reported in the table summaries. The women were between the ages of twenty-five and thirty-eight years. Pelvic operations were necessary and the date of the operation was fixed at a desired time after the expected ovulation. Of these selected cases, those are reported which were found to have a fresh corpus luteum of ovulation. During the course of the operation this corpus luteum was removed.

Following this ablation of the corpus luteum, two types of treatment were given. In the first series, the patients were treated with estrin (progynon benzoate),* receiving with one exception 10,000 rat units (50,000 international units) daily. Characteristic menstrual flow began after a lapse of two to five days after excision of the corpus luteum, thus taking place before the time of the next expected period. In one case a dosage of 20,000 rat units (100,000 international units) was given daily. Bleeding began on the sixth day following excision of the corpus luteum. Thus, in these cases, as in the experiments on monkeys, estrin did not inhibit bleeding from a secretory endometrium.

In the second series, progestin† instead of estrin injections were begun at time that the corpus luteum was excised.

In the first three of these cases, an inadequate dosage of progestin was given (0.5 Rb. U. daily) and bleeding occurred on the second, third, and fourth days, respectively, after the removal of the corpus luteum. In two subsequent cases, a much larger dosage of progestin was given (Table I), and bleeding was held in abeyance beyond the next expected period. After ten days of replacement therapy, eleven days after the removal of the corpus luteum, endometrial biopsies were taken. A secretory endometrium was found. Typical bleeding occurred two and four days after cessation of progestin therapy. In one of these cases, No. 13, the patient gave a history of dysmenorrhea. At about the expected time of bleeding, she reported severe cramps and the subjective feelings of imminent menstruation. Treatment was continued for three days further but no spotting occurred. Bleeding began four days after the last day of the injections, seven days after the subjective symptoms of expectance. This was a longer cycle than this patient had reported before the operation.

SUMMARY

The clinical cases herein reported confirm for the human being the observations made on the monkeys in regard to the rôle of estrin and

*We are indebted to Dr. Erwin Schenk of Schering-Kahlbaum and Co., for furnishing part of the progynon B for these studies.
†Progestin (Organon), 1 c.c.=1 International Unit.

progestin in menstruation. Estrin, even in massive doses, does not prevent menstrual bleeding in the presence of a progravid endometrium if the corpus luteum is ablated. Bleeding may be inhibited after removal of a corpus luteum, for the duration of the treatment by an adequate amount of progestin. Bleeding in these cases occurs shortly after cessation of the progestin treatment, which in our cases was some days after the next expected period.

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TWISTED HEMATOSALPINX COMPLICATING PREGNANCY

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MEDICAL literature is replete with references to torsion of normal and pathologic fallopian tubes, both before and after puberty, but relatively few cases of torsion of these tubes occurring during pregnancy have been recorded. This paper is concerned with a review of the cases of torsion of hematosalpinx complicating pregnancy, and with a report of one such case recently seen in our own clinic. All cases of hematosalpinx caused by ectopic pregnancy have been excluded. Since our case contributes nothing additional to the various controversies concerning such questions as torsion of normal versus torsion of abnormal tubes; the formation of hydrosalpinx before hematosalpinx; and the mechanisms of torsion, it is felt that it would be of no value to recount the discussion in the literature on these points.

After a careful search only 13 cases of twisted hematosalpinx complicating pregnancy could be found. These are summarized in Table I. In addition to these, several other cases are mentioned even though our original criteria would exclude them from this group.

Peraire[11] reported a case of torsion of hydrosalpinx without hematosalpinx. In the cases of Schoenholz[16] and Routh,[15] the tube was not twisted and collections of blood in the involved tubes were found. Hubrich[7] reports an interesting case of intrauterine pregnancy complicated by a twisted hematosalpinx due to an old tubal abortion. Sheldon[17] reports a case of complete torsion of the right tube and ovary complicating a three months' pregnancy, but does not directly state that hematosalpinx was present. This particular patient aborted on her third postoperative day.

CASE REPORT

Mrs. H. M., a white nineteen-year-old primigravida, entered the University Hospital Nov. 24, 1935, complaining of pain in the right lower abdominal quadrant associated with nausea and vomiting. It was noted upon admission that the patient was about thirty-eight weeks pregnant.

The family history was negative. In the past year's history, the patient described vague irregular pains in the lower right quadrant of the abdomen, and these episodes

TABLE I

AUTHOR	YEAR	DURATION OF PREGNANCY	AGE OF PATIENT	SYMPTOMS	PREOPERATIVE DIAGNOSIS	SIDE INVOLVED	OVARY INVOLVED	SIZE OF TUMOR	EFFECT OF OPERATION ON PREGNANCY	REMARKS
1. Hartmann[6]	1898	5-6 mo.	20	Pain, vomiting, distention	Peritonitis	R	Yes	Not stated	Went to term	
2. Praeger[14]	1899	4 mo.	35	Pain, constipation, urinary retention	Ovarian cyst on twisted pedicle	L	No	10 by 10 by 7 cm.	Not interrupted	
3. Pinard and Paquy[13]	1901	4 mo.	26	Pain, nausea, vomiting, distention, icterus	Ovarian cyst on twisted pedicle	R	Ovary enlarged	8 by 4 by 3 cm.	Went to term	
4. Pinard[12]	1902	Term	36	Pain, nausea, vomiting, distention	Not stated	R	No	Size of orange		Operation 6 hr. after delivery. Mother recovered
5. Aullhorn[2]	1910	3 mo.	19	Pain, rigidity	Pyosalpinx	R	Swollen	9 cm.	Simply states "recovery"	
6. Ward[21]	1910	4 mo.	20	Pain, nausea, vomiting, rigidity, fever	Acute appendicitis	R	Not stated	Filled abdomen	Went to term	

TABLE I—Cont'd

7. Lecene[8]	1912	5 mo.	21	Pain, nausea, vomiting, tenderness, rigidity	Appendicitis	R	No	Not stated	"Recovery"	
8. Eastman[4]	1927	7½ mo.	23	Pain, nausea, vomiting, tenderness	Acute appendicitis	R	Yes	"Massive"	Went to term	
9. Dell[3]	1928	7 mo.	24	Pain, nausea, vomiting	Appendicitis	R	No	"Large"	Went to term	
10. Green-Armytage[5]	1929	6 mo.	16	Pain	Acute appendicitis	R	Yes	6½ cm.	Went to term	
11. Stevens[19]	1930	8½ mo.	33	Pain, nausea, vomiting, tenderness	Acute appendicitis	R	Not stated	"Hen's egg"	Cesarean section at time of operation	Live baby. Mother recovered
12. McKerrow[10]	1934	6 mo.	30	Pain, tenderness	Not stated	R	Not stated	"Infant's fist"	Went to term	
13. Taubenhaus[20]	1934	3 mo.	34	Pain, nausea, vomiting	Ovarian cyst on twisted pedicle	L	No	"Hen's egg"	Therapeutic abortion 13 days after operation	Patient recovered
14. Savage	1935	38 wk.	19	Pain, nausea, vomiting, tenderness, rigidity	Acute appendicitis	R	No	7 by 6 by 6 cm.	Went to term	

had been thought by her physician to be mild attacks of appendicitis. The menses began at thirteen years of age and had always been regular and normal in every respect. There was no history of vaginal discharge or other symptoms of gynecologic importance. The last menstrual period had occurred on Feb. 25, 1935, and the estimated date of confinement was Dec. 4, 1935.

The pregnancy had been entirely uneventful until one week previous to admission when the patient experienced a sudden, moderately severe pain in the right side of the lower abdomen accompanied by nausea and vomiting. The patient was confined to her bed most of this week with remissions and exacerbations of these symptoms. On Nov. 23, 1935, there was a sudden intense pain in the right lower quadrant of the abdomen with marked increase in the nausea and vomiting. A white blood cell count at this time showed 11,000 cells per c.mm. of blood, and expectant treatment was followed. Since there was no improvement by the following day, hospitalization was advised and accepted.

Upon admission the patient was seen to be about thirty-eight weeks pregnant with the uterine fundus 30 cm. above the symphysis pubis. Her expression reflected pain and anxiety, and she was slightly more comfortable with the right thigh flexed upon the abdomen. Her face was flushed; respirations were 28 per minute; the pulse was 100 per minute; and the temperature 99° F. General physical examination was negative except for the abdominal findings as follows: the uterus was normal for a pregnant uterus, in size, shape, and consistency and was not tender; the fetus was found to be presenting L.O.T., the fetal heart was normal; and there were marked tenderness, rigidity, and muscle spasm most marked at a point in the right midaxillary line where this line would be bisected by a line drawn transversely about 3 cm. above the umbilicus.

Laboratory findings on admission were: a normal blood picture except for an increase in white blood cells to 17,000 per c.mm., and a 90 per cent concentration of polymorphonuclear cells; sedimentation rate was moderately increased; and two catheterized specimens of urine were entirely negative. A tentative diagnosis of acute appendicitis complicating pregnancy was made, although the possibility of torsion of an ovarian cyst on its pedicle was considered, and immediate operation was advised and accepted.

Upon opening the abdomen through a high right McBurney incision, a small amount of cloudy serous fluid was expressed, and a reddish purple, firm, and somewhat friable mass the size of an orange was encountered. This mass was seen to be the dilated distal portion of the right tube twisted clockwise once with the point of torsion about 2 cm. from the uterine end, and it was removed in the usual manner. The right ovary was normal in every respect and was not removed. The appendix was mesocecal, not inflamed or enlarged, but slightly adherent to the wall of the uterus, and because of this close proximity to the uterus, it was not removed. The abdomen was closed without drainage. The postoperative course was entirely uneventful, and the incision healed by first intention.

Uterine contractions began Dec. 3, 1935, nine days after operation, and after a labor of twenty-four hours which was complicated by cervical dystocia and maternal and fetal distress, the patient was delivered by internal podalic version and breech extraction following episiotomy and Dührssen's incisions in the cervix. The child was a normal, full-term, living female weighing 6 pounds 9 ounces (3,150 gm.). The puerperium was entirely normal, and the patient and her baby were discharged from the hospital in good condition on Dec. 15, 1935.

Pathologic examination of the right tube was made by Dr. C. G. Warner of the Department of Pathology who reported the following: The gross specimen was the distal 8 cm. of the right tube including a cystic mass 7 by 6 by 6 cm. It was a deep reddish purple color with prominent small vessels under the serosa. The peritoneal surface was smooth and glistening with no apparent inflammatory reaction.

There was a small cyst 1.0 cm. in diameter, close to the fimbriated extremity. On longitudinal section, the dilated tube contained a serous bloody fluid with some clots. The lining was somewhat trabeculated and was roughened by deposits of blood and pigment. The wall was 1.0 mm. thick about most of the periphery. The vessels on section were thrombotic. Microscopic examination showed hemorrhage into the wall of the tube and in the folds of the mucosa. Careful search revealed no evidence of tubal pregnancy.

NOTE.—Mrs. H. M. was readmitted to the University Hospital Nov. 18, 1936. The patient had been well since her discharge from the hospital in December, 1935. The last menstrual period was Feb. 19, 1936, and the estimated date of confinement Nov. 26, 1936. Her prenatal course was uneventful and was under the supervision of Dr. B. P. Warren. Labor began on Nov. 17, 1936, and after eleven hours the cervix was completely dilated. On Nov. 18, 1936 the patient was delivered of a full-term, living male child, weighing seven pounds thirteen ounces, L.O.A., by means of low forceps following an episiotomy. The third stage was uneventful. Inspection of the cervix revealed a laceration in the midline posteriorly about 6 cm. in length; this was immediately repaired. The total duration of labor was eleven and one-half hours. The immediate puerperium was entirely uneventful.

SUMMARY

1. Thirteen cases of twisted hematosalpinx complicating pregnancy are summarized from the literature; and a new case is added.

2. The condition occurs in young women; the youngest and oldest in this series were sixteen and thirty-six years, respectively.

3. Nine cases occurred before the seventh month of pregnancy.

4. The commonest symptoms were lower abdominal pain on the side involved, and nausea either alone or accompanied by vomiting.

5. The preoperative diagnosis was erroneous in each case. The commonest preoperative diagnoses were acute appendicitis and twisted ovarian cyst, in the order named.

6. In 12 out of the 14 total cases the right tube was involved, or in 85.7 per cent.

7. The size of the tumors in this series varied from that of a ''hen's egg'' to that of a mass filling the transverse width of the lower abdomen.

8. In 11 cases the pregnancy was not influenced and went to term. In Pinard's[12] case the patient was operated upon six hours after delivery; cesarean section was performed at the same time in the case reported by Stevens,[19] and Taubenhaus[20] resorted to the therapeutic abortion in his case, thirteen days after removal of the tube, because of the exhaustion of the patient.

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MEDICAL ARTS BUILDING

COMPARATIVE STUDY OF PELVIC TEMPERATURES UNDER VARIOUS THERAPEUTIC PROCEDURES*

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FOR the past several years much has been written about the use of heat as a therapeutic measure in pelvic infections. On our service at Lincoln Hospital we have employed the three types most commonly used, diathermy, Elliot treatment, and for the past year, the short wave radiotherm. This latter machine has a nine-meter wave length with an output of 200 watts. We became interested in knowing just what heat penetration was obtained with the three different methods.
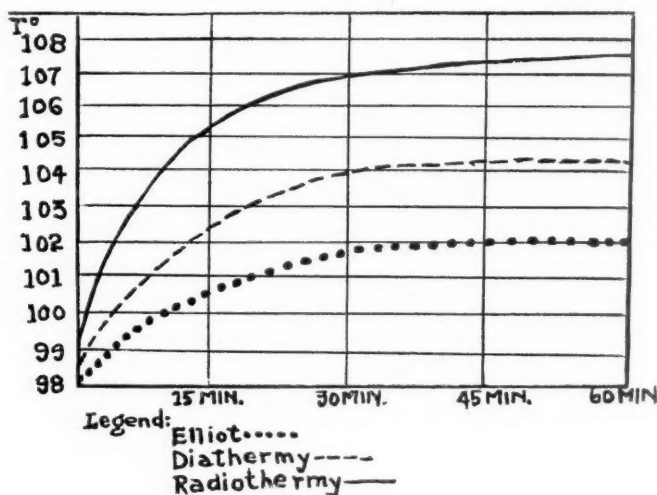
Fig. 1.—Intrauterine temperatures obtained under various therapeutic procedures.

The following procedure was carried out: The patients used were those who prior to the trial had dilatations and curettages done for incomplete abortions. A silk bougie was passed through the cervix to the fundus of the uterus. In the diathermy and radiotherm treatments a vaginal applicator was then applied and the other electrode was placed on the abdomen just above the symphysis. In the Elliot treatment, after introducing the silk bougie into the uterus, the vaginal applicator was inserted. These treatments were all given for an hour. Temperature readings were taken at different intervals by means of introducing a thermocouple through the inserted silk bougie. No patient was given more than one treatment daily, although several of the patients were used for all three methods of treatment.

In our eighteen cases studied, several interesting facts were found.

First, that the size and obesity of the patient apparently has no bearing upon the intrauterine temperature obtained.

Second, that the highest cervical temperature which the patient will tolerate comfortably is 110° F.

Third, that this cervical temperature was obtained with the radiotherm in approximately five minutes; with the diatherm in about ten minutes, and with the Elliot treatment, which never reached above 109° cervical temperature, in about one-half hour.

Fig. 1 shows the intrauterine temperatures obtained. It was interesting to note that all of these temperatures reached the normal level in about five minutes after the treatment was discontinued.

DISCUSSION

DR. PAUL L. WERMER.—Dr. Ingraham neglected to remark that we reached temperatures of 107° F. at the fundus of the uterus by means of the radiothermy device. This evidently meant that heat was being effectively transmitted to the fundus and probably to the tubes. The temperature attained was thus close to the thermal death point of the gonococcus.

The machine we used was a nine-meter affair with compensator, computed to have a 200 watt output and 400 to 500 input. The thermocouple was of constantine and copper and sheathed in a No. 8 English catheter. The voltage generated was measured by a sensitive millivoltmeter capable of accurate readings at 1/100 of a millivolt.

DR. FRANCIS W. SOVAK.—With the use of the Elliot machine I had the opportunity to take some temperature readings during a laparotomy and at that time found the temperature of the culdesac 6° higher than normal and the temperature about the liver 1° higher than normal. The different temperatures in the peritoneal cavity were ascertained after the Elliot bag was in the vagina forty minutes.

DR. HENRY D. FURNISS.—The reason Dr. Sovak got his 6° rise was because he probably had the culdesac and the uterus isolated from the rest of the peritoneal contents, thus preventing dissipation of heat. Is that correct?

DR. SOVAK.—We simply made a small incision and inserted the thermometer before making the incision to get into the peritoneal cavity.

DR. FURNISS.—Herrick of Los Angeles did some experimental work along this line. He claims that with the Elliot apparatus and the bag in the vagina one never gets a temperature of over 102° in the uterus or the urethra. With very low frequency and ordinary diathermy you get the greatest degree of heat at the region of the greatest electrical resistance. If you place one electrode on the skin of the abdomen and one over the back the current does not necessarily go straight through from the one to the other; it may go around. To get the heat effect, one of the electrodes must be in one of the orifices, such as the urethra, the cervix, or the vagina.

DR. INGRAHAM (closing).—I think the temperature that Dr. Sovak obtained in the culdesac is easily accounted for, as the culdesac is practically in apposition to the vaginal applicator of the Elliot machine. Thus it is practically the cervical temperature which we give as 109°.

TUBOOVARIAN PREGNANCY

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THIS case is the only tuboovarian pregnancy thus far observed at the Woman's Hospital.

Halban-Seitz **Handbuch,**[1] discussing tuboovarian pregnancy, prefers to call it "ovary-tube" pregnancy and states that such is only possible if both the tube and ovary take part in the formation at the site of the implantation. He believes there must have been a preexisting fusion of the tube and ovary before impregnation. Furthermore, the fimbriated end of the tube may spread out over the ovary and become sealed to it, or the fimbriated end of the tube may close off entirely and the ovary become fused to the tube at an accessory lumen. No matter which method of sealing the tube to the ovary takes place, the follicle can ripen immediately below the lumen (in one case the fimbria and in the other the accessory) and the ovum in either case has access to the crate of the follicle. After fertilization occurs, implantation may occur either on the tubal portion of the "ovary-tube" lumen or canal, or on the ovarian portion, and the distinction can be made as either primary tubal or primary ovarian "ovary-tube" pregnancy. Schumann,[2] in an excellent treatise on extrauterine pregnancy, states that one deals with a tuboovarian pregnancy when the fetal sac is composed partly of tubal and partly of ovarian tissue. The fimbriated end of the tube has previously to be adherent to the ovary.

The patient, white, American, twenty-three years of age, began to menstruate at eleven years of age, every twenty-eight days for four days. No pain or clots. Last period Oct. 23, 1933. Married three years. One full-term pregnancy one year ago, normal delivery and puerperium. Pneumonia at sixteen years. Entered the Out-Patient Department on Jan. 18, 1934, where a diagnosis of probable ectopic pregnancy was made and she was immediately admitted. Her chief complaint was that twenty days after she began to menstruate she had vaginal spotting for sixty-seven days. She complained of occasional mild cramplike pains in the left lower quadrant. A month before she had a fainting spell. Examination revealed a normal well-developed woman. The pelvic floor was slightly lacerated but had good function. The cervix was one and a half times normal size. The uterus, anterior and to the right, was twice normal size, with a possible myoma. A diagnosis of intrauterine pregnancy was made, since practically no tenderness was elicited on examination. An ectopic was scarcely suspected. Urine negative. Blood, R.B.C. 3,900,000; Hg 85; W.B.C. 11,200; polymorphonuclears 72; lymphocytes 28. Wassermann negative. Sedimentation time: first hour 22 mm. (82 min.). An Aschheim-Zondek test was positive. A consultant stated: "pregnancy (ectopic?), mass behind the uterus and to the left side. Diagnosis, threatened abortion? Watch and wait. Examine frequently." On the eighth day after admission, not because of any pain or any fainting, but because the staining still persisted and the mass on the left side seemed to be increasing, the patient was operated upon.

Operation.—Cervix soft and firmly closed. Uterus had a measured depth of 11 cm., was pushed over to the right and contained a large amount of decidual tissue. There was a boggy cystic mass about 10 cm. in diameter in the left adnexal area, part of which was ovary and part tube. This was apparently an ectopic which had ruptured through the fimbriated portion of the tube, not unlikely into one of the ovarian cysts,
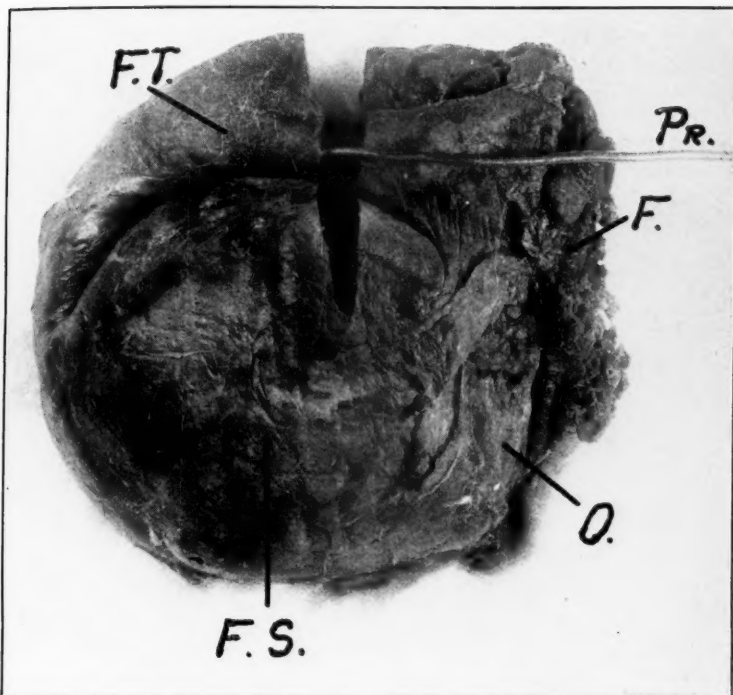
Fig. 1.—*F.T.*, Fallopian tube. *Pr.*, Probe in ostium fallopian tube. *F.*, Fimbriae fallopian tube. *O.*, Ovary. *F.*, Fetal sac.
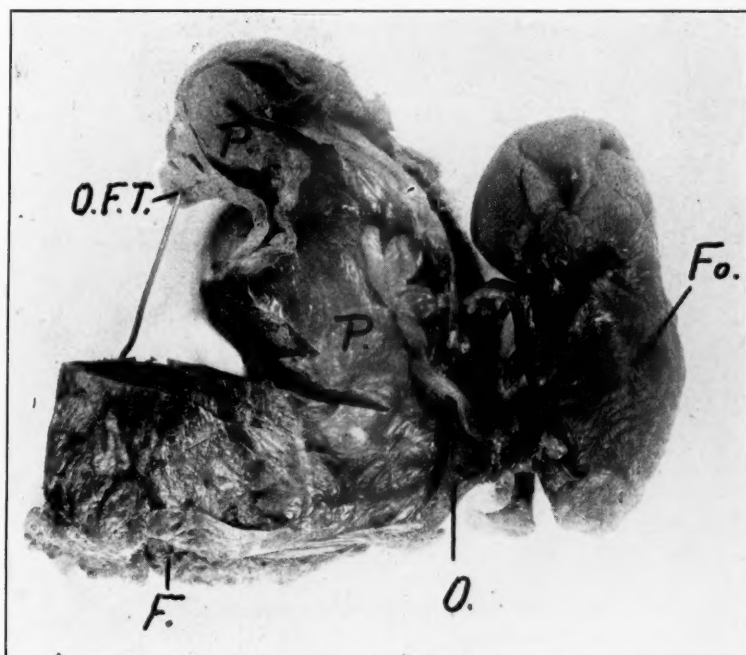
Fig. 2.—*P.*, Placenta. *F.*, Fimbriated fallopian tube. *Fo.*, Fetus. *O.*, Ovary. *O.F.T.*, Ostium fallopian tube.

but it could not be definitely made out where the ectopic insertion was. There were about 300 c.c. of clotted blood in the culdesac, and from 150 to 200 c.c. of fluid blood free in the abdominal cavity. There were no adhesions except that the whole mass was adherent to the posterior wall of the uterus and to the culdesac by light adhesions, probably organizing blood clot.

Frozen section revealed decidua but no malignancy, and no evidence of chorionic elements. The abdomen was then opened by a low transverse incision and left
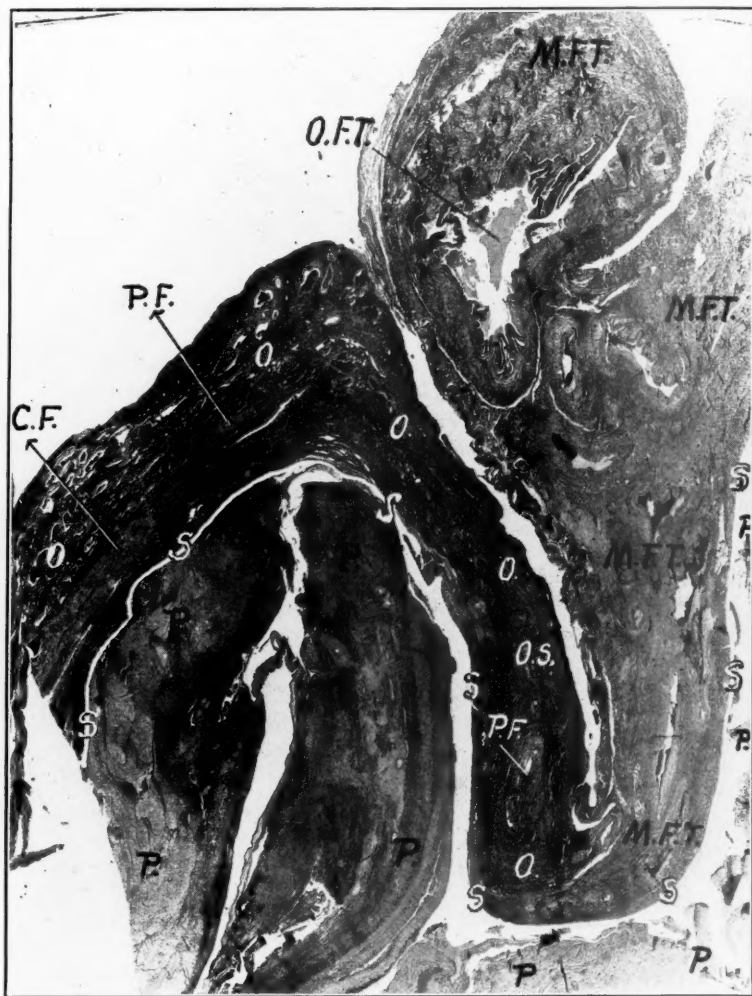
Fig. 3.—*P.*, Placenta. *O.*, Ovary. *S.*, Placental attachment. *O.F.T.*, Ostium fallopian tube. *M.F.T.*, Muscle fallopian tube. *O.S.*, Ovarian stroma. *C.F.*, Corpus fibrosum. *P.F.*, Primordial follicle.

salpingo-oophorectomy done. Anesthesia: Nitrous oxide, oxygen and ether. Preoperative blood pressure 100/40. Postoperative blood pressure 96/55. Time of operation: one hour 2 minutes. On the same day the patient was given a transfusion of 450 c.c. of blood by the Scannell method. She had a normal convalescence, her incision having healed by primary union, and she left the hospital on the eighteenth day in good condition.

Pathologic Findings.—The curettings were composed of well-developed decidua without any evidence of degeneration. Chorionic elements were not detected. The abdominal specimen (Figs. 1 and 2) (macroscopic) consisted of a pregnancy sac 9 by 6 cm. in diameter, to which was attached an isthmic portion of the tube 5 cm. long, extending from the upper margin of the cystically distended ampulla to the abdominal parieties. The tube wall was missing at about half of the surface and the edges of the preserved tube wall revealed previous rupture. Old blood was accumulated between the contents of the cystic portion and the tube wall. Fresh blood was clinging to the outer surface. The fetal sac was intact, except for some fragmented chorion which hung loosely from the opening. The amniotic fluid was clear. The embryo, a normal male, measured 12.5 cm. The umbilical cord was tortuous, formed two large varicosities 1 cm. from the embryo. The ovary could be separated from the tube wall only in its upper margin, while its lower part was fully incorporated in the tube wall. Its approximate size following outlines was 5.5 by 4.0 cm.

Incision through the sac: A cut exposing the wall of the fetal sac revealed it furnished both by the tube and by the ovary, the one transgressing into the other without obvious limit. Thus, only the proximal third of the tube was preserved while the distal portion was completely used up in the formation of the fetal sac. *Microscopic* (Fig. 3): A section through the deep notch in the wall of the fetal sac revealed it composed on one side by atrophic or stroma including compressed atrophic graafian follicles and corpora fibrosa, and on the other side by stretched atrophic tube wall with small remains of the mucosa. The fetal sac was incompletely intercepted by the described fold formed by ovarian tissue and tube wall at the side of their junction, simulating two fetal cavities. In both partitions, the fetal layers were well preserved except for both areas where hemorrhage had occurred between the area of nidation and the chorionic structures. The chorionic tissue showed extensive fibrosis of the stroma of villi. Sections of other parts of the cystic cavity revealed similar pictures. *Diagnosis:* Tuboovarian pregnancy, twelve weeks of age, unruptured. Intrauterine decidua.

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79 EAST NINETY-FIRST STREET

Seguy and Isidor: Pseudo-Pregnancy and Sterility, Gynécologie (Paris) 34: 281, 1935.

Ordinarily a delay in menstruation of two or three weeks in women who are habitually regular is considered as due to an early abortion. However, in the presence of our new knowledge concerning hormones such a diagnosis should be made with caution. The authors report a series of cases where menstruation was delayed and they believe the delays were due to a disturbance in the rhythmic and successive action of follicular and luteal hormones on the uterine mucosa. Such disharmony may produce a decidual reaction in the absence of a fertilized ovum. In the authors' cases they could not prove their contentions but as probable evidence they cite the fact that the biologic reactions of the urine were negative and the delay in menstruation was seen in some women whose husbands have azoospermia. In cases of pseudo-pregnancy and sterility it is important to rule out ectopic pregnancies. This can readily be done by means of urine tests. Ordinarily it is believed that a hypersecretion of progestin delays menstruation, but the authors believe that follicular cysts may produce the same results by bringing about a temporary polyhormonal amenorrhea.

J. P. GREENHILL.

FATAL AIR EMBOLISM ON THE EIGHTH DAY OF THE PUERPERIUM

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FATAL embolism resulting from the entrance of air into the veins of the uterus has been described many times as a result of attempts at criminal abortion, less frequently as a complication of labor at full term and in these cases usually immediately postpartum. In many, some condition was present necessitating interference such as placenta previa or postpartum hemorrhage.

Gough[1] reported air embolism in a woman of twenty-five in her second labor. Forceps delivery had been done for prolapsed cord when the anesthetist reported that the patient had collapsed. The pulse, unobtainable at the wrist, was 170 obtained from the abdominal aorta, dyspnea was marked, the patient in extreme pallor, cyanosis developing just before death. The patient regained consciousness for a time, then coma supervened. Restlessness was extreme, requiring restraint, death occurred seven hours after delivery.

Autopsy showed the right ventricle markedly dilated, with flabby walls which appeared transparent. Opened under water the right ventricle was found to contain much free air and a little frothy blood. The pulmonary arteries also contained frothy blood; there were no thrombi.

One other case was found in the literature of a fatal air embolism as late as the eighth day postpartum after a normal labor and puerperium. This case was reported by May in the *British Medical Journal*, June 6, 1857.

Symptoms described in the collected cases were: A sense of oppression about the chest, a feeling of sinking or exhaustion, extreme restlessness, dyspnea and faintness, convulsive movements were noted in two. Pallor was noted in many cases and in a few cyanosis was a terminal symptom. Death was immediate in 17 cases, after "several hours" in two cases, after five hours in one case, less than one hour in one case, "after a short time," one case.

Three died in physicians' offices after attempts to produce abortions.

It is evident from the literature that the occurrence of death from air embolism as a complication of an otherwise normal pregnancy, labor, and puerperium and occurring as late as the eighth day postpartum is very rare and merits an additional case report.

L. M. H., hospital number 89052. This twenty-six-year-old housewife, a gravida iv, was first seen in the Rochester General Hospital prenatal clinic, Sept. 1, 1935. Her last menstrual period was May 11, 1935, and was normal in character. Up until the time she was seen her pregnancy was uneventful. Her family history was essentially negative. Her father died of typhoid fever. Her mother and one sister were living and well. The patient had typhoid fever at three years of age, measles and whooping cough in childhood. She had frequent attacks of tonsillitis as a child. Tonsillectomy at six years of age. No illness since that time. Her periods were regular, with some pain the first two days. Moderate flow.

She has had 3 previous pregnancies, 2 of which were uneventful and terminated in spontaneous deliveries of normal living children. Had normal puerperiums after both deliveries, the last one in January, 1933. The third pregnancy terminated at home in a spontaneous abortion at three months.

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On October 22, 1935, she was admitted to the obstetric service because of premature rupture of membranes (sixth month of pregnancy).   She complained of some low backache which she had had for about five weeks.   She presented no toxic symptoms.   Blood pressure was 110/68.   No edema.

The fetus was active.   Vaginal examination the day after admission showed that the head was not engaged and that the cervix was closed and not effaced.

She had no vaginal drainage after admission to the hospital.   She had an attempted medical induction of labor with castor oil and quinine which was not successful and she was discharged three days after admission to be followed in the prenatal clinic.   She continued to have some watery vaginal discharge at intervals and some backache but no other complaints.   On Jan. 1, 1936, she was again admitted to the obstetric service because of the onset of pains which were mild and recurred every fifteen minutes.   She had no vaginal drainage or discharge at this time.

Examination at this time revealed nothing of note.   Her blood pressure was 110/86.   Urine was negative.   Rectal examination showed that the head was not engaged but that the cervix was patulous but not effaced.   Pains ceased soon after admission and she was again given castor oil and quinine but did not go into active labor and was discharged on the third day to the prenatal clinic.

She was seen each week and on Jan. 23 she had again lost considerable fluid and had been having some bloody show for three days.   She was again admitted and labor was induced.   She went into labor and delivered spontaneously, after an eight-hour labor, of a 6 pound, 12 ounce normal female child (vertex R.O.A.).   Very little postpartum bleeding.

Following delivery she ran a perfectly normal postpartum course.   Her temperature was never above 98.6° F.   Lochia was normal and at no time abnormally profuse.   Her breasts began secreting on the fourth day.   On the seventh postpartum day she was in knee-chest position thirty minutes in the morning and afternoon.   On the morning of her eighth postpartum day she was again put in knee-chest position.   She had been up in the position five minutes when, without any outcry or warning, she fell out of bed.   When the nurse, who was in the ward at the time, reached her she was pulseless, gasping for breath, and had an ashen, cyanotic color.   She was seen by a house officer about five minutes later but by this time her respirations had ceased and heart sounds could not be obtained.   A clinical diagnosis of massive pulmonary embolism was made.   Autopsy was obtained and done four hours after death.

Report of Autopsy Findings.—The body was that of a well-developed, well-nourished white female, twenty-six years of age.   Breasts well developed and contained milk.   Abdomen was that of a postpartum patient.   Uterus could be felt just below the symphysis pubis.   No edema or scars of lower extremities.

Chest: There was a small amount of clear pericardial fluid.   The *heart* was in normal position.   The right ventricle was much distended, it was ballooned up and on palpation felt like being full of air.   The pulmonary artery was distended and seemed to contain air.   When the pericardial sac was filled with water in situ and the right ventricle opened, a large amount of air escaped and also a small amount of frothy red foam.   The right auricle, ventricle, and pulmonary artery contained no postmortem blood clots, no blood clot emboli, only very little frothy blood.   The left ventricle and aorta contained no air.   Myocardium, endocardium, and valves were normal.   Coronary arteries were patent.   The aorta was normal.   *Lungs* showed some acute emphysema, otherwise normal.   Abdomen: Liver, gallbladder, spleen, kidneys, adrenals, and pancreas were of normal size and position, and they showed nothing abnormal.   Stomach and intestines were also normal.   The *right ovarian plexus* was much distended and filled with a great many air bubbles.   The left ovarian plexus, however, did not seem to contain air.   Uterus measured 12 by 16 by 8 cm. and was about the size of a newborn's head, definitely subinvoluted.   Section revealed hypertrophied, but otherwise normal muscle tissue without the slightest evi-

dence of crepitation. The uterine cavity appeared to be moderately distended and contained about 60 to 80 c.c. of dark red liquid blood. Attached to the posterior wall and adherent to it was another brownish red blood clot, 10 by 5 by 2 cm. in size, apparently with beginning organization. This old blood clot was covered by several fresh dark red blood clots which were very easily removable. At the lower pole of

Fig. 1.—Retained small pieces of decidua tissue surrounded by blood clot.
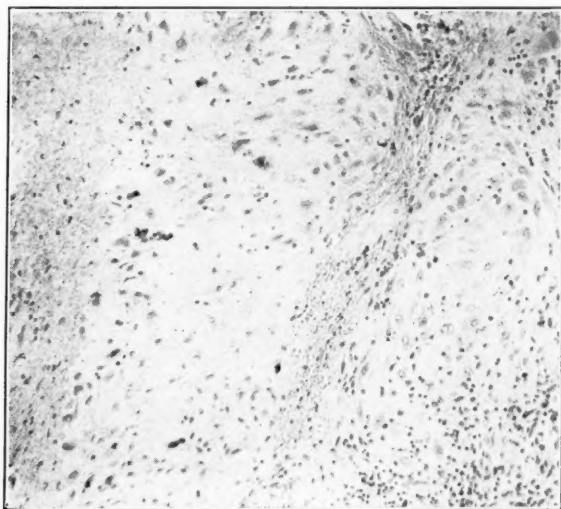
Fig. 2.—Same as Fig. 1, but with higher magnification.

the old clot was another fresh clot which was lying free in the cavity (Fig. 1). The lower pole of the old blood clot was separated from the uterine wall. Upon raising this part of the old clot, three freely gaping, patulous sinuses, about 3 or 4 mm. in diameter, could be seen. There were clots in the other sinuses in that region. The rest of the uterine surface was smooth and showed no signs of infection.

Ovaries, tubes, bladder, and *rectum* showed no remarkable pathology. *Histology:* Several blocks were cut at different levels from the uterus in the region of the adherent blood clot. In these sections *retained decidua tissue* with some chorionic villi was found surrounded by blood clots and hemorrhages (Fig. 2). In the uterine wall just beneath this area there were much distended uterine veins filled with thrombi and some of these showed early organization. Blocks were also examined from other parts of the uterus. In these regions there was no evidence of endometritis, there was no necrosis of the muscle and there were no gas bubbles in the wall.

Anatomic Findings.—(1) Moderately subinvoluted uterus eight days postpartum. (2) Retained small pieces of placental tissue with surrounding hemorrhages and blood clots. (3) Sudden death due to air embolism at the time of changing knee-chest position. Air was sucked in probably through the opened large uterine veins. (4) Dilatation of heart, right ventricle, due to the presence of much air. (5) Marked distention of right ovarian plexus due to abundant air bubbles.

Cause of Death.—(1) Fatal air embolism by way of opened uterine sinuses. (2) Retained small pieces of decidua tissue with hemorrhage.

In this case it is easy to reconstruct the mechanism of this accident. There evidently had been some bleeding from the placental site due to the retained small particles of decidua tissue. Blood clots were formed not only around the retained small pieces of decidua tissue but also in numerous uterine veins just beneath this area. As the patient went into the knee-chest posture, the lower pole of this blood clot became separated from the uterine wall and several large veins became opened. At first hemorrhage occurred which was suddenly followed by the suction of air into these gaping veins in sufficient quantity to block the pulmonary artery and the right side of the heart.

The case is that of a real air embolism, in which the origin of the embolism from gas bubbles, produced by bacterial agents, was sufficiently ruled out.

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Gardner, Smith, Allen, Edgar, and Strong: Cancer of the Mammary Glands Induced in Male Mice Receiving Estrogenic Hormone, Arch. Path. **21**: 265, 1936.

Mammary cancer develops spontaneously in female mice of certain strains; it seldom or never occurs in males. Feminization of the male mouse by ovarian grafts induces a partial growth of the mammary glands. Mammary cancer can be induced in male mice receiving estrogenic hormone over an extended period. The development of mammary cancer appears to be a sex-limited character in the mouse. The following experiment was made: Two of six male mice from one litter of the A strain were subjected to weekly injections of 500 international units of keto-estrin benzoate in oil. Two carcinomas developed in one mouse and one in a second mouse. The female mice of this strain are susceptible to spontaneous mammary cancer. The pattern of mammary growth induced in these animals was abnormal in that the growth of the duct system was restricted or stunted and the mammary lobules developed extensively. This work has been verified further by additional animals showing the same results. These tumors appeared in mice at ages varying from 162 to 362 days and after the mice had received from 10,000 to 18,000 international units of keto-estrin benzoates. Four of the mice were under 200 days of age at the time that the tumors were observed.

W. B. Serbin.

A FULL-TERM PREGNANCY COMPLICATED BY AN ACUTE INTESTINAL OBSTRUCTION AND FALSE LABOR PAINS*

JOHN CASAGRANDE, M.D., BROOKLYN, N. Y.

ACUTE intestinal obstruction complicating pregnancy is relatively rare. Bemis[1] states that only 13 cases were reported in the American and British literature from 1900 to the time of his report in 1931. Since this time I have found only four other reported cases, including his, one each by Cornell[2] and Blair,[3] and one by Kornfeld and Daichman.[4]

At the Brooklyn Hospital we have had two cases of acute intestinal obstruction complicating pregnancy in 11,246 cases, covering a period of ten years.

The present case is reported because it presented an interesting problem in diagnosis as well as a difficult decision on the time for surgical intervention in view of the uncertain status of labor.

The patient was a twenty-nine-year-old para ii. Her prenatal record showed nothing of interest. Her previous history included a laparotomy in 1926 in Norfolk, Virginia, performed for chronic appendicitis, a cystic right ovary, and a retroversion of the uterus. The appendix and right ovary were removed and a Crossen's suspension of the uterus was done, the round ligaments being shortened by sewing them to the posterolateral surface of the uterus, thus correcting the retroversion and at the same time utilizing them to peritonealize the raw surfaces. One week after discharge she was readmitted for an incision and drainage of an ischiorectal abscess. In 1929 she had an uncomplicated delivery of a full-term fetus at the Brooklyn Hospital.

The patient's present history began two days before admission, at which time she appeared in the emergency ward of the Brooklyn Hospital, complaining of lower abdominal pain. The examining interne made a diagnosis of impending labor complicated by a degenerative fibroma. She refused admission and signed a release form, and several hours later the pain subsided spontaneously. Two days afterward, however, at 3:15 P.M. on October 15, 1935, she was admitted to the obstetric service, complaining of intermittent cramplike pains in the lower abdomen occurring at intervals of ten to fifteen minutes, which began at 12:15 P.M. the same day.

It was assumed that she was in labor. Her last period had occurred Dec. 28, 1934, making her theoretically overdue eleven days. Four hours after admission, it was reported that the patient was having severe bearing-down pains and, as no presenting part could be felt in the brim, a malpresentation or position was suspected.

Examination at this time showed an uncooperative highly nervous patient, complaining of irregular intermittent pains in the lower abdomen. Her general condition was good. Her temperature was 97°, pulse rate 80, and blood pressure 110/70. The urine showed a faint trace of albumin, with a two-plus acetone and a few hyaline and granular casts. She had vomited a small amount of bile soon after admission and had had two spontaneous bowel movements that morning.

The abdominal examination disclosed a full-term pregnancy. The fetal heart rate was 128, heard best in the right lower quadrant. Strong uterine contractions lasting forty seconds were recurring every four to five minutes. There was a soft, tender, compressible mass, dull on percussion, extending from the pubes and left groin to just below the umbilicus. Vaginal examination showed an unengaged vertex presenting, the cervix was open one finger but not effaced, and the membranes intact. It was at first thought that the mass might be a distended bladder, mis-

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placed as a result of her previous pelvic operation, and so the patient was catheterized and four ounces of urine obtained, with no effect on the mass.

The patient at this time began to get drowsy and her pain disappeared, probably as a result of morphine given one hour previously. It was accordingly decided to reexamine her in two hours to determine whether the patient was having a false or true labor. The effect of the morphine soon wore away and the severe pains and strong uterine contractions returned, but since there was no further dilatation of the cervix, it was assumed that the patient was having a false labor and that sur-
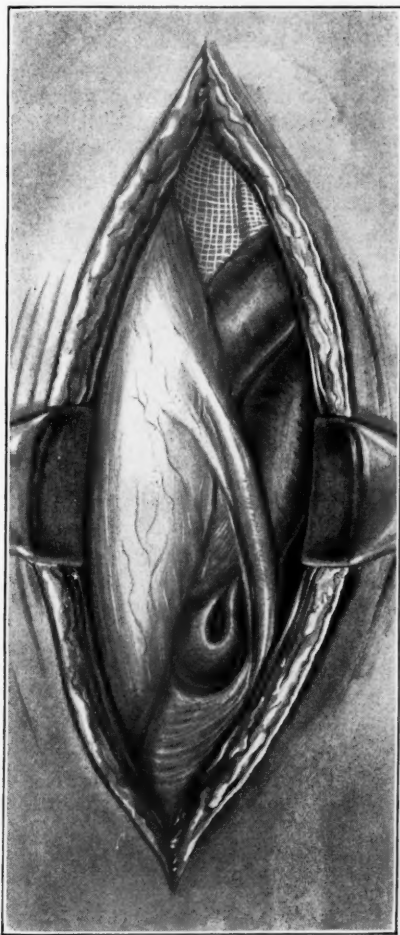
Fig. 1.—Showing a portion of strangulated ileum passing through a rent in the left broad ligament just beneath the round ligament.

gery might be indicated for the tumefaction. A blood count at this time showed 95 per cent hemoglobin, 4,800,000 red blood cells. There were 19,900 leucocytes with 95 per cent polymorphonuclears, and 5 per cent small lymphocytes. Immediate operation was decided upon after further surgical and obstetric consultation, because of the uncertain status of labor.

The patient was then given $\frac{1}{4}$ gr. of morphine by hypodermic and a 1500 c.c. clysis, preparatory to laparotomy. At the operation it was found that six to eight inches of what appeared to be devitalized ileum had passed through a rent in the peritoneum just beneath the previous operative attachment of the left round

ligament. The rent in the broad ligament was obliterated by suturing. The devitalized ileum was brought through a stab wound preparatory to an ileostomy which was done thirty hours later. Following the laparotomy she was given generous doses of pantopon with the hope that labor would be delayed at least twenty-four or forty-eight hours. Her immediate postoperative reaction was satisfactory.

The onset of labor occurred at 1 P.M., October 17, 1935, thirty-six hours after operation. A Beck binder was applied, pantopon given for analgesia, and the patient was told not to bear down. Three hours later she was fully dilated, the membranes were ruptured artificially, and the vertex engaged in the brim in an R. O. P. position. Under gas oxygen and ether anesthesia an unsuccessful attempt to rotate the head anteriorly with the Kielland forceps was made. The Dewees' forceps were then applied, and after considerable traction the vertex was brought down to the pelvic floor and a Scanzoni maneuver was done just as the vertex reached the perineum, thus converting an R. O. P. into an R. O. A. The Elliot forceps were then used to complete the delivery of a normal baby, weighing 8½ pounds. No lacerations resulted. Her postpartum convalescence was uneventful. The mother and baby were discharged sixty-one days after admission.

COMMENT

The error in assuming that this patient was in labor on admission is readily understandable since she was at term, in fact theoretically past due, and she had definite uterine contractions which increased in frequency and duration.

In reading over reports which closely parallel this case, I have noted that uterine contractions simulating labor pains were common enough frequently to mask the true diagnosis. I venture to say that labor would have begun sooner in this case had the obstruction not been relieved. Just why uterine contractions simulating labor pains in this case and others paralleling it, occur, is apparently not known. In this patient it was probably direct irritation caused by the strangulated gut, part of which was in direct contact with the anterior surface of the uterus.

The report of the interne was incorrect when he thought that there was a malposition or presentation because the presenting part was not entering the pelvis, even though the patient was apparently having very hard bearing down pains. But this observation was important, as it led to a more intensive survey and surgical consultation, with the much needed operative intervention.

After the decision to operate was made, two problems were discussed. The first was whether the patient was actually in labor, and, if so, would she deliver in a matter of a few hours? The surgeon would have risked delaying the operation a short time, if we could have assured him of a relatively quick vaginal delivery. Since we could not do this, the other problem arose, namely, should pregnancy be terminated by cesarean section and followed by whatever other surgery was indicated, or should the necessary surgery be done and the pregnancy allowed to terminate via the natural passages? In general the principle of treating complications and allowing nature to take care of the pregnancy seems wise, and I believe this principle is generally accepted.

The exception to this would be in the very rare cases where an obstruction of the sigmoid is caused by direct pressure of the gravid uterus or the presenting part as it crosses the pelvic brim, as in the case reported by Blair. It is obvious that a cesarean section would then be a proper expedient to relieve the obstruction.

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30 PIERREPONT STREET

TWO CASES OF UNRUPTURED ECTOPIC PREGNANCY*

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(From the Department of Surgical Pathology of the Cook County Hospital)

THESE two cases of unruptured ectopic pregnancy are being presented because of the diagnostic difficulties encountered, the large size of the specimens, and their association with salpingitis.

CASE 1.—Colored female, aged thirty-nine years, gravida i, para 0, had a spontaneous abortion three years prior to admission to the hospital, and now entered complaining of pain in the right lower quadrant for eighteen days. The onset had been ushered in with vague abdominal distress, followed after four days by severe sticking, knifelike pains in the right lower quadrant, lasting for a few hours and then replaced by a generalized cramping pain, the latter lasting for a few days. The pain again localized to the right lower quadrant where it remained up to her admittance to the hospital. A venereal history was denied, but the patient stated that a discharge had been present since her marriage.

Her menstrual periods had been regular up to December, 1935, when they became irregular and more frequent. That month she had two periods, the first coming at its regular time, lasting three days with a moderate flow, and the second fifteen days later, lasting only one and one-half days with a scanty flow. In January she again had two periods, at approximately the same time, the first period lasting five days with the flow quite profuse for the first three days, the second lasting again five days but the flow quite scanty. Dysmenorrhea was not present at any time.

Physical examination revealed a well-nourished, well-developed colored female who did not appear acutely ill. Temperature was 99.8°, pulse 88, respirations 20, and blood pressure 116/82. The abdomen was somewhat distended with moderate rigidity over the lower quadrants and tenderness in the lower abdomen, more marked in the right lower quadrant. Pelvic examination revealed a moderate, foul discharge. The tip of the cervix was somewhat softened. An elongated irregular mass was felt in the right adnexal region extending from the uterus and quite tender. Laboratory findings were essentially negative. The impression at that time was a chronic salpingitis with tuboovarian abscess, though an incomplete tubal abortion had to be considered.

At operation the uterus was found softened and fixed by adhesions in the pelvis and the middle two-thirds of the right fallopian tube was converted into a mass 6 by 5 by 4 cm., soft and purplish red. The fimbriated ends of both tubes were occluded and the left tube was thickened. On sectioning this mass, a cavity 3 cm. in diameter was exposed and was found to be filled with a yellowish fluid and adherent to the lining by a stalk was a 13 mm. fetus approximately five to six weeks old. The wall of the sac was 9 mm. thick and dark purple gray.

CASE 2.—A white female, aged thirty-six years, gravida iii, para iii, whose last child was born in 1933, entered the hospital because of abdominal pain of five weeks' duration and vaginal bleeding. Language difficulty resulted in a rather meager history. Indefinite abdominal pain had been present for the past five weeks, being dull, aching in character with occasional sharp pain in the left lower quadrant. A venereal history was denied. Her menstrual periods had always been regular until December, 1935, when she missed a period. In January she menstruated scantily for two days. On the morning of admission she had had slight vaginal bleeding.

*Presented at a meeting of the Chicago Gynecological Society, March 20, 1936.

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Physical examination revealed a well-nourished, well-developed, white female of thirty-six years, who did not appear acutely ill. Temperature was 100°, pulse 88, respirations 18, and blood pressure 118/70. Pelvic examination revealed that the cervix was firm and closed, the uterus slightly enlarged and deviated to the right. A hard nodular mass was palpated in the left adnexal region and not attached to the uterus, but pushing it to the right. No tenderness was elicited. The laboratory findings revealed a normal blood count (white cells 9,800, red cells 4,000,000, and hemoglobin 80 per cent). X-ray of the abdomen showed a small amount of air underneath the right diaphragm. Wassermann test and urine were negative. The impression at this time was that of an ovarian cyst with functional bleeding. An ectopic pregnancy had to be ruled out and an exploratory operation was advised.

At operation the left fallopian tube at its isthmic portion was found converted into a mass 7 by 6 by 5 cm., deep purplish red and soft. The distal portion of the tube was fused with the ovary to form a mass 6 by 5 by 1 cm. and was markedly thickened. On section of the larger mass, the wall was found to be up to 2 cm. in thickness, and a cavity was exposed lined by a purple brown membrane and attached to this by a stalk was a 10 mm. fetus about four to five weeks old.

Of added interest in conjunction with the two cases just presented is an analysis of 50 cases of ectopic pregnancies encountered by the Surgical Pathology Department of Cook County Hospital in 1935. A correct diagnosis was made in 70 per cent of the cases, while in the unrecognized ones, the most common diagnosis was a chronic salpingitis. Appendicitis, ovarian cysts, and pelvic peritonitis followed in the order named. Of these 50 cases, 32 per cent were found to be ruptured at operation. Salpingitis, which is thought to be a common finding, especially in those patients seen at Cook County Hospital, was present in only 16 per cent of all the cases, the diagnosis being based on gross and microscopic findings at the site of gestation.

Cook County Hospital

EMPHYSEMATOUS VAGINITIS

Jason H. Robberson, M.D., Amarillo, Texas, and May Owen, M.D.,
Fort Worth, Texas

EMPHYSEMATOUS vaginitis, or colpitis emphysematosa, is a rare condition that occasionally occurs during pregnancy. Ingraham and Hall recently reviewed the literature and reported three cases.*

We are presenting a case in which this unusual condition occurred twice within a period of two years. Both clinical and histologic studies were made, but no cultures or examinations of the gas content of the cysts were carried out.

Mrs. M. M. was first seen in April, 1932. She was then twenty-four years old and had been married three years, with no pregnancies. Her chief complaint was dysmenorrhea for the past twelve months. During the past four months she had noticed that immediately following each menstrual period she would have an irritating discharge, scant in amount. Concurrent with the discharge small white blisters would appear on the labia, accompanied by considerable itching and burning. The blisters would disappear in from one to three days to recur following the next menstrual period. There was no discharge or other discomfort between periods.

Examination, revealed innumerable small blebs or blisters, in the fornices of the vagina, with a greater number on the posterior wall. These were small distended

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*Ingraham, Clarence B., and Hall, Ivan C.: Am. J. Obst. & Gynec., 28: 772, 1934.

cysts in the mucosa of the vaginal wall and cervix. The cysts were discrete, firm, and could not be displaced as in subcutaneous emphysema. They occurred in clusters, interspersed with normal-appearing vaginal mucosa. A fold of mucosa on the right posterolateral wall was studded with the gray, glistening cysts. Tissue was removed from this fold of mucosa for pathologic study. The pathologic report follows:

The biopsy specimen consisted of two slightly wedge-shaped cystic pieces of tissue. Both pieces floated partially submerged when placed in water. One surface of each
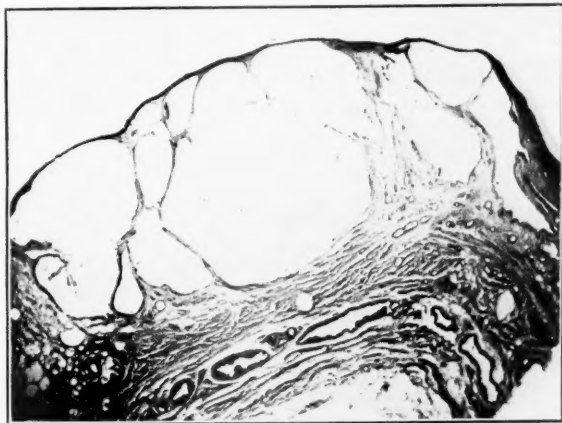
Fig. 1.—Section showing large spaces or vesicles just beneath the mucous membrane; mucous gland tubules in deeper layers of tissue.

Fig. 2.—Section showing vesicle wall of fibrous tissue without lining cells.

piece was covered with multiple small cysts or blisters that varied from pinpoint to 8 mm. in diameter. The small cysts lay just beneath the mucous membrane and when broken, made a slight noise. The vesicles were empty. The largest piece of tissue measured 2.5 by 2 by 1 cm. Histologic examination revealed loose fibrous connective tissue, one surface being covered with a thin layer of well-differentiated squamous epithelial cells. Just beneath the epithelium were multiple, small varying sized spaces that had no definite lining cells. The surrounding fibrous tissue was

edematous and in some areas diffusely infiltrated with lymphocytes and a few leucocytes. A number of thin-walled blood vessels were present but were not distended with blood.

The patient was instructed to use alkaline douches, and for several months following the removal of the biopsy there was no recurrence of the vesicles. The vaginal discharge continued, however, and on May 27, 1933, the cervix was cauterized; at that time no blisters were seen.

Early in 1934 the patient became pregnant and was under the care of one of us from February through May. On May 9, 1934, she had a spontaneous abortion following vaccination for smallpox. During this pregnancy there was no noticeable recurrence of the emphysematous cysts. In September, 1934, the patient was again pregnant, and at that time there was a recurrence of the emphysematous cysts. On October 15 and again on October 31 it was necessary to open as many of the large blisters as possible for relief of pressure of which the patient complained. This time the cysts were more marked on the anterior vaginal wall. The cysts continued to recur, and it was necessary to open them at intervals of four to six weeks in order to relieve the discomfort in the vaginal canal. Jan. 10, 1935, the patient had a spontaneous premature labor and delivered a five months' fetus which showed signs of heartbeat for thirty minutes but never breathed. The placenta contained a large hematoma. It was the obstetrician's opinion that the premature labor was due to an abruptio placentae. When she was examined six weeks postpartum no cysts were present, and all pelvic symptoms had subsided.

This patient was examined in September, 1936, and no traces of blebs were found.

LITHOPEDION

S. A. OSHEROFF, M.D., OMAHA, NEB.

(From the Department of Obstetrics and Gynecology, Creighton University)

MRS. D., aged twenty-eight years, came to see me on Feb. 28, 1935, with the following complaint: vaginal bleeding, commencing in the middle of December and continuing daily up until the present time, which has not been profuse at any time nor was it accompanied by pain. She passed a few small clots. Her menses had been regular and normal up until September. She missed her periods in October and November, started to flow in December and kept it up.

She had been married for ten years and had conceived and miscarried about nine years ago.

She stated that she had considerable pain in her right side during her pregnancy which was terminated after four months by a spontaneous abortion.

She had a rather prolonged convalescence, but in six weeks she was up and around attending to her usual household duties. However, the pain and tenderness in the right side continued, and lately she noticed a tender lump in her lower abdomen to the right.

The physical examination was negative, except for pale and anemic appearance. Cervix normal, uterus small, showing two nodules on the opposite lateral surfaces, a little above and to the left a large cystic mass could be felt, which was not tender, spherical in shape and extending upward to the superior spine of the ilium; it was slightly movable. On the right side of the uterus, about one inch medial to McBurney's point, there was another mass about the size of a large hen's egg, rather hard to the touch and quite tender, and it was somewhat fixed.

A diagnosis was made of fibrotic uterus, ovarian cyst on the left, possible pedunculated adherent fibroid on the right. She was sent to the hospital and operated upon on March 2, 1936. Under evipal and ether anesthesia the abdomen was opened in the midline. A hard calcified mass was found the size of a large hen's egg, firmly adherent to the omentum and fimbriated end of the right tube. It was lying anterior to the uterus and about three inches above and lateral to it. Upon palpation one could easily feel the grating of bones inside the calcified sack. The mass was removed without difficulty and was found to contain a fetal skeleton about the size of a four and one-half months' pregnancy.

On the left side an ovarian cyst, the size of a medium-sized grapefruit, was found with the tube distended and completely adherent to the cystic mass. This was also removed. The uterus was of normal size but contained fibrotic nodules at both cornua. As this made it useless from a reproductive standpoint, it was thought best to remove it and thus obviate the possibility of another operation if the fibroids should happen to grow.
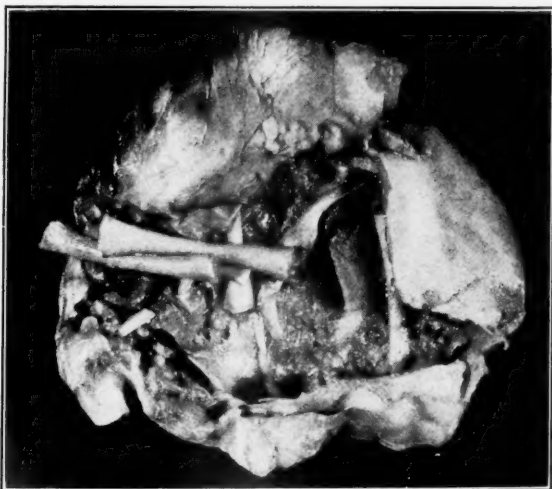
Fig. 1.

The right ovary looked fairly normal, and it was preserved. Prophylactic appendectomy was done. The abdomen was closed in the usual manner.

Histopathologic Examination: The tubal mass measured 6 by 5 by 5 by 4 cm. and had the feel of a cracked eggshell. On cut section it showed a lining of flat bone and contents of grayish yellow grumous material with numerous spicules of bone, having the appearance of long bones, tibia, femur, and humerus. The uterus measured 7 by 5.5 by 3 cm. showing marked hyperplasia of the lining and hemorrhagic at the cornua of the left tube. There was a small subserous fibroid at the right tube and a small chocolate cyst, having the appearance of an endometrial implant. The ovarian cyst with attached tube was 8 cm. in diameter, with thin walls and serous yellow fluid contents. *Microscopic:* The uterine wall was thickened and fibrosed. The mucosa showed marked hyperplasia and hypertrophy with twenty or more acini in the low power field. There was no evidence of any malignancy.

Diagnosis: (1) Benign hyperplastic endometritis, (2) lithopedion, and (3) simple unilocular cystadenoma of left ovary.

The postoperative course was uneventful, patient leaving hospital on the twelfth day.

In viewing this case in retrospect, it is evident that this was a case of right tubal pregnancy, occurring nine years previously, followed by abortion of fetus into the abdominal cavity, and formation of adhesions between fetal sac on one side and omentum and fimbriated end of tube, on the other, continued growth of fetus until the fourth month of gestation, with death and calcification following.

236 MEDICAL ARTS BUILDING

COLLECTING A CLEAN URINE SPECIMEN

B. H. CARROLL, M.D., TOLEDO, OHIO

DR. LITT* described the use of an adaptor for collecting urine from women under aseptic conditions. Any procedure which lessens the number of catheterizations is of great importance. In using the adaptor several disadvantages developed. The glass of an ordinary adaptor is fragile and easily broken. The pressure required in applying the adaptor about the opening of the urethra is often sufficient to prevent the act of urination. The presence of a nurse to hold the adaptor may defeat its purpose.
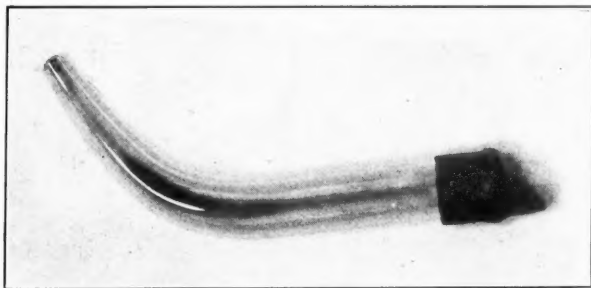
We have had an adaptor of similar size made up from Pyrex glass and therefore not easily broken.† A collar of soft rubber is fitted about the neck with a visor or shield 1 cm. long extending forward on the anterior surface to direct the flow of urine into the tube.

After cleansing the patient as for catheterization, the labia are separated and the adaptor with rubber collar is placed about the opening of the urethra. The labia are allowed to fall around or grasp the rubber collar and hold it in place. A small basin is placed for the urine as it comes from the adaptor. Proper draping should be arranged over the patient and the nurse may leave the room, if necessary.

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*Litt: AM. J. OBST. & GYNEC. 30: 433, 1935.
†Made by Rupp & Bowman Co. Toledo, Ohio.

PREGNANCY AFTER THE REMOVAL OF BOTH OVARIES

W. A. Scott, M.B., F.R.C.S., Toronto, Canada

(From the Department of Obstetrics and Gynecology, University of Toronto)

THE difficulty of devising any method for the certain sterilization of a patient is well recognized, but ordinarily it is thought that where both ovaries have been completely removed, future pregnancies will not occur. There are, however, a few cases on record where this is not true, and in 1902 Doran* reviewed previously reported cases and reported one of his own.

It may be noted that in most of the reported cases there was some difficulty in dissecting out the ovaries, and consequently there was a possibility that some normal ovarian tissue was left. There is always the possibility, however, that in these patients there is accessory ovarian tissue which possibly occurs more frequently than we are accustomed to think.

The case that I wish to report must be put down to the presence of unrecognized accessory ovarian tissue, as there was no possibility of any tissue being left from either of the normal ovaries. The patient was thirty-one years of age and had three normal full-term children. Ten months after her last confinement a solid tumor of the left ovary the size of an orange was discovered. During the next month this was obviously increasing in size and on Feb. 28, 1934, the abdomen was opened and this tumor was found to be a freely movable dermoid of the left ovary. At operation a dermoid of the right ovary the size of a lime was discovered which had not been felt previous to operation. It appeared to be impossible to leave any normal ovarian tissue and consequently both tumors, which were free from adhesions, were removed, the outer half of each tube being removed with the corresponding ovary. The tubal stumps and the pedicles were ligated with catgut. Six weeks after operation the patient developed well-marked menopausal symptoms, consisting of hot and cold flushes, nervousness and other evidence of vasomotor disturbances. These symptoms continued for about three months at which time the patient had a slight menstrual flow and the menopausal symptoms disappeared. Menstruation then continued at about six-week intervals until Jan. 15, 1935.

In May the patient returned for examination because there was no further menstruation and was found to be pregnant. This pregnancy progressed in an uneventful manner and the patient was delivered of a full-term child on Nov. 9, 1935. The baby was not nursed and menstruation has not recurred and the menopausal symptoms have returned to a slight degree.

At the time of operation no accessory ovarian tissue was seen, but it is obvious that it must have been present. It is of interest, however, that when the patient was examined on Jan. 22, 1935, before it was known that she was pregnant, a note was made of a small movable mass the size of a filbert low down in the right fornix. The note states that "this feels like a small ovary." It cannot be felt at the present time, March, 1936.

I believe that this case must be accepted as a pregnancy occurring from accessory ovarian tissue which did not at first function, but which after the removal of the other ovary gradually became functioning tissue.

*Doran, Allen: Obstetrical Transactions 44: 231, 1902.

CARCINOMA OF THE CERVIX IN PROLAPSED UTERI

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(From the Surgical Service, Brooklyn Cancer Institute)

CARCINOMA of the cervix in association with procidentia is a very rare condition, as attested by Guthrie and Bache, who in 1932 made an extensive review of the literature, supplemented with a questionnaire sent to the leading clinics and gynecologists throughout the United States. They found not a single instance had been reported in the entire French literature nor had other outstanding European gynecologists seen a case. The late J. G. Clark, shortly before his death, stated that he had never seen the two conditions in the same patient. Judd of the Mayo Clinic saw three cases of cervical cancer out of 2,188 procidentias, while Graves saw only one case out of 683 patients. Pomtow reviewing the literature up to 1893 found only 29 cases recorded. There are probably not over 70 cases noted to date, and since all of these are not reported (most were elicited by questionnaire), there may be a certain amount of overlapping. I feel that this case is both rare and interesting enough to be noted, as it represents the only case that I have encountered in the 700 consecutive cervical cancers personally observed.

Mrs. A. S., a Swedish widow of seventy-six years, was admitted to the Clinic on May 4, 1934, complaining of leucorrhea and vaginal bleeding for the past six months, and a "fallen womb for nine years." The menopause occurred twenty-six years ago. The patient had had four full-term spontaneous deliveries. The pertinent physical findings were mitral and aortic stenosis, associated with a mild hypertension. Vaginal examination revealed a complete procidentia. The cervix at its most dependent portion presented an ulcerated, eroded area measuring 3 × 3½ cm. which was firm in consistency and bled on manipulation. This ulcerated area was surrounded by a zone of induration.

At this same visit, a biopsy was taken which revealed on microscopic examination changes in the prickle cell layer of the epidermis, with an unrestrained growth of cells. The neoplastic cells occurred as large compact masses, some of which were undergoing degenerative changes, presenting cystic-like formation. Clumps of these cells were observed within lymphatic channels. There was a slight tendency toward keratinization. The stroma was the seat of leucocytic infiltration.

Diagnosis: Prickle cell carcinoma.

Through some oversight the patient was admitted to the hospital twenty days later without any radiation at all and had a vaginal panhysterectomy done. Report of the specimen confirmed the original biopsy findings. The patient was discharged from the hospital on the thirteenth day, after an uneventful convalescence, except for a vesicovaginal fistula, which occurred at the operation. Follow-up a year and a half later revealed the vaginal vault to be high, free from any malignant recurrence, with a persistent fistula which the patient refused to have corrected.

This case is reported through the courtesy of Dr. John J. Gainey.

755 OCEAN AVENUE

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE MEDICOLEGAL ASPECTS OF BLOOD GROUPING

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THE discovery of the blood groups in 1900, 1901 by Karl Landsteiner[1,2] not only made blood transfusion—hitherto a therapeutic fantasy—a feasible and valuable procedure, but also opened up a completely new field in blood research, which in the short space of a year yielded its first medicolegal fruits. Thus, in 1902, Landsteiner and Richter[3] demonstrated the possibility of identifying the blood groups from bloodstains, and of applying this knowledge in those cases where bloodstains of either the criminal or victim had been left at the scene of a crime.

In 1910, von Dungern and Hirszfeld[4] demonstrated the hereditary nature of the four blood groups, and advocated the application of this knowledge in forensic cases for the exclusion of paternity. According to these workers the agglutinogens A and B were transmitted as Mendelian dominants, by two independent pairs of allelomorphic genes, so that the agglutinogens could not appear in the blood of a child unless present in the blood of one or both of its parents.

The inheritance of the blood groups has been corroborated by all subsequent workers, but in 1925, Bernstein[5] proposed a new theory of transmission which conformed much more closely with statistical expectancies and with the data which had accumulated during the preceding period of fifteen years. This theory is now universally accepted. According to Bernstein's theory, the blood groups are inherited by means of three allelomorphic genes, A, B, and R. This theory supplies another postulate which is important for the exclusion of paternity, namely, that a group AB parent cannot have a group O child, and a group O parent cannot have an AB child, a situation which could occur were the von Dungern and Hirszfeld theory correct.

By this time the legal machinery had been started on the continent, and through the work of Schiff in Germany and Lattes in Italy, the isoagglutination tests were gradually being accepted in the courts as evidence in cases of disputed paternity. According to statistics compiled by Schiff,[6] by 1929 the tests had been used in as many as 5,000 cases in the various countries of Europe.

Meanwhile, further developments had taken place in the serologic phases of blood grouping. In 1911, von Dungern and Hirszfeld[7] had succeeded in demonstrating that there are two sorts of agglutinogen

A, subsequently designated A_1 and A_2 by Landsteiner and Levine. With their aid, the individual differences in human blood were increased to six, namely, O, A_1, A_2, B, A_1B and A_2B, so that the possibilities for criminal identification were greater. Although the hereditary nature of the subgroups of Group A and Group AB is now generally recognized, certain technical difficulties make their forensic application unsafe for the time being.

The discovery by Landsteiner and Levine in 1927[8, 9] of the M and N properties of human blood and the fact that these, too, were inherited gave further impetus to the new branch of forensic medicine, and by 1932, this knowledge was being applied in European courts. Up to that time, although a large part of the pioneering in this field of research had been done in America, its recognition as a reliable criterion in forensic medicine was confined almost exclusively to European countries. In 1930, the famous Bamberger-Watkins case occurred in Chicago.[10] In this case the accidental interchange of two newborn infants in a hospital, rectified by the use of the blood groups, did much to focus the attention of both the medical and legal professions on the possibilities of these discoveries. The next case occurred in New Haven in 1933,[11] and this time the blood groups were used successfully to effect an exclusion of paternity. Progress was slow, however, and certain legal difficulties still barred the way to universal adoption of the test.

In 1934, at a meeting of the American Medical Association, following an address by Karl Landsteiner,[12] a resolution was passed to acquaint the legal profession with the reliability of these tests, so that steps might be taken to facilitate their application in forensic cases. Hitherto, this type of evidence was admissible, but the courts did not have the authority to compel the parties in an action to submit to the examination against their will.[13] On March 22, 1935, laws were passed in New York State giving the courts of that state the power to order blood tests in cases where the question of paternity or maternity was relevant to the issue. Shortly thereafter similar laws were passed in Wisconsin, and probably the other states will follow suit. According to the existing laws in New York State,[14] the defendant in a paternity proceeding now has the right to demand a blood examination to establish his innocence.

The results of such tests are of value only for purposes of exclusion, as when a particular combination of blood types in the putative father, mother, and child is incompatible. On the other hand, compatibility is of no positive value. Because of the limited number of blood types, there is a possibility of coincidence. For example, the falsely accused man and the father could belong to the same blood type. In Wisconsin[15] the statutes are so framed that evidence based on blood grouping is admissible only if an exclusion of paternity or maternity is definitely established. As stated before, the Bernstein theory postulates that the blood groups are transmitted by three allelomorphic genes. Corresponding to the four blood groups, six genotypes are possible (see Table I). On this basis, it is a simple matter to deduce what groups are possible in the children, when the groups of the parents are given. For example, if the father belongs to Group AB, and the mother to Group O, half of the sperm will carry gene A, and half gene B, whereas all the ova will carry the gene R. Equal num-

TABLE I. BERNSTEIN'S THEORY OF HEREDITY OF THE BLOOD GROUPS

PHENOTYPE	GENOTYPE	
	HOMOZYGOUS	HETEROZYGOUS
AB		AB
A	AA	AR
B	BB	BR
O	RR	

bers of zygotes must be of genotypes AR and BR, so that half of the children will belong to Group A and half to Group B. In a similar manner, the other nine matings possible can be analyzed (see Table II).

TABLE II. THE BLOOD GROUPS IN PARENTS AND CHILDREN

GROUPS OF PARENTS	GROUPS OF CHILDREN POSSIBLE	GROUPS OF CHILDREN NOT POSSIBLE
O × O	O	A, B, AB
O × A	O, A	B, AB
O × B	O, B	A, AB
A × A	O, A	B, AB
A × B	O, A, B, AB	—
B × B	O, B	A, AB
O × AB	A, B	O, AB
A × AB	A, B, AB	O
B × AB	A, B, AB	O
AB × AB	A, B, AB	O

A study of Table II shows that: (1) The agglutinogens A and B cannot be present in the blood of the offspring unless present in the blood of one or both parents. (2) An AB parent cannot have an O child. (3) An AB child cannot have an O individual as one of its parents. As an ancillary test, Schiff[16] has pointed out that if the corpuscles of the infant are agglutinated by the serums of both parents, then nonpaternity is established, except in the case where the child is of Group AB and the parents of Groups A and B, respectively.

Since the possibility of distinguishing two genotypes depends on the relative frequency of all genotypes in the population, and this frequency varies in different localities, the chance of effecting exclusion of paternity also varies in different localities. Wiener[17] has shown that, using the four blood groups, the chance of effecting an exclusion of paternity ranges between 16 and 19 per cent for most localities. These figures refer to the chance of excluding paternity if the defendant is actually innocent. In actual practice, however, the percentage is lower, since many of the defendants are not entirely blameless. If the individual, unjustly accused, belongs to the Group AB, he has two chances in five of proving his innocence. The individual of Type O comes next with one chance in five. The B type is less fortunate, with only one chance in seven, whereas the A individual is truly unfortunate, should he be falsely accused of paternity, since his chances are only one in thirteen.

If only one of the parents is available, a serologic examination of his or her blood and that of the child may yield pertinent information, but naturally the chances are less than when both parents are tested. This circumstance may arise, for example, in cases where the husband suspects infidelity, but prefers to gather further evidence before con-

fronting his wayward spouse; or when one of the parents is dead. If the man or woman is shown to belong to Group AB and the child to Group O, or the supposed parent to Group O and the child to Group AB, parentage is immediately excluded.

With the discovery of the M and N properties of human blood, the serologist's scope was further increased. The agglutinogen N has no natural agglutinin, and only one case has been described in which natural agglutinins for M were present in human blood.[18] Antiserums can be prepared, however, by immunizing rabbits with M and N blood. From these, testing fluids are made which give specific agglutination reactions for M or N, similar to those of the blood groups A and B.

The agglutinogens M and N are inherited as simple Mendelian dominants, by means of a single pair of allelomorphic genes, M and N. The following genotypes are, therefore, possible: MM, NN and MN, corresponding to the three known types M, N and MN, respectively. By reasoning, similar to that used for the blood groups, one can determine to what type or types the children from any mating must belong (see Table III).

TABLE III.   THE HEREDITY OF MN TYPES OF LANDSTEINER AND LEVINE

MATINGS	GROUPS OF CHILDREN POSSIBLE	GROUPS OF CHILDREN NOT POSSIBLE
M × M	M	N, MN
N × N	N	M, MN
M × N	MN	M, N
M × MN	M, MN	N
N × MN	N, MN	M
MN × MN	M, N, MN	—

From Table III it follows that: (1) The agglutinogens M and N cannot appear in the blood of the child unless present in the blood of one or both parents. (2) Two parents belonging to Type M cannot have Type N children, and parents of Type N cannot have Type M children. The frequencies of the three types in the general population are approximately: M, 30 per cent; N, 20 per cent; and MN, 50 per cent. An innocent man of Type M or N has about one chance in three of clearing himself, whereas the MN type has no chance whatever. A falsely accused man of undetermined type has approximately one chance in six of proving nonpaternity by exclusion. By combining the blood groups and MN types, the chances of disproving paternity have been increased to one in three.

The following case illustrates how this knowledge can be applied.*

In September, 1935, a woman in Buffalo, New York, sued her husband for separation, while he countered with a suit for annulment of marriage on the basis of fraud. The facts were that up to the time of the trial she had been in the state of matrimony seven times. During the sixth venture, she had had an affair with her present husband, and the child in question was supposed to be the fruit of that clandestine union. However, the defendant denied that the child was his; in fact, he asserted that it was not even his wife's, insisting that he had been inveigled into his marriage by that pretext. In the court it was shown that the child and putative father both had a "curly large toe," and the plaintiff's counsel made capital of

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*I am indebted to Dr. A. S. Wiener for the details of this unpublished case.

this observation. Eventually a blood test was ordered by the court, and the following results were obtained: mother, AN; putative father, BM; and the child, BM.

From this it can be seen that the woman could not possibly have been the mother of the child. This conclusion is based upon the law that a Type N parent cannot have a Type M child, the result of the classic blood grouping tests being inconclusive. Incidentally, evidence was presented at the trial to show that the plaintiff had had a salpingectomy and an ovariectomy performed in 1916. The woman explained her midline scar by asserting that she had had her present child by cesarean birth, although she could not produce the surgeon who was supposed to have performed the operation. However, the former husband testified that the plaintiff had not been pregnant at the time the child was born; in fact, she had never menstruated as long as he knew her. Finally the true father was located, and it was learned that he had left the child at the same orphan asylum from which the plaintiff had adopted it.

Here is a case of a carefully planned fraud which might have succeeded had it not been for the use of the blood grouping tests.

Experience over a period of twenty-five years has shown that these tests are completely reliable in the hands of the expert serologist. Since the fate of several people depends upon the decision, it is essential that the person performing the tests be well experienced in the technic. For this reason, the court should permit only physicians appointed by authoritative medical councils with expert genetical advice to undertake the examinations.

As mentioned before, there are two sorts of agglutinogen A, namely, A_1 and A_2. The agglutinogen A in Subgroups A_2 and A_2B reacts more weakly than the corresponding agglutinogen in Subgroups A_1 and A_1B. The agglutinogen is not infrequently so weak in Subgroup A_2B, that errors may result in inexperienced hands. As a rule, the weaker types are readily recognized, but when the sensitivity of the corpuscles is less than usual, and a serum of low titer is used, the reaction will be missed. Therefore, it is essential to use only serum of high titer, using both A_1 and A_2 blood as controls. By doing each test at least in duplicate, using different serums for each set-up, the chances of error are further minimized. As an additional control the unknown serums should each be tested against known cells of Groups O, A_1, A_2 and B.

The agglutinogens are already present in the blood of the child at birth, and whatever agglutinins are present in the serum were derived from the mother by filtration through the placenta. During the first few weeks of life, these agglutinins gradually disappear to be replaced by the permanent agglutinins of the individual. Pari passu with these changes the sensitivity of the agglutinogen increases, until it reaches its maximum strength in early adult life. It is evident, therefore, that it is unwise to apply these tests too early in life, particularly if the child belongs to either Group A_2 or A_2B. In competent hands, however, a reliable result can be obtained as early as the second week of life.

Recently, Friedenreich[19] demonstrated the existence of a rare type of N agglutinogen, designated by him as N_2. This type is very much weaker than the common agglutinogen N, designated by Friedenreich as N_1. The agglutinogen N_2 is especially weak in the presence of M, so that blood MN_2 could be wrongly diagnosed as M. Due regard to the precautions previously outlined is the only way of avoiding this pitfall.

In conclusion, it should be pointed out that proper precautions should be taken to identify the individuals presenting themselves for the test. Whenever possible, the plaintiff and the defendant should identify each other before the samples of blood are taken. In addition, some permanent record should be kept, either by means of photographs or fingerprints, in order to forestall any attempt at substitution.

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Lesnoi, S. K.: Disorders of Menstrual Function Due to Atresias and Cervical Stenosis After Induced Abortion and Operative Delivery. Vopr. Endocrinol, Moskow, p. 913, 1936.

The trauma inflicted during the performance of an artificial abortion leads at times to the firm concentric and excentric atrophy of the uterus. Some writers see the danger in a hormonal trauma, due to interruption of the trophic influence of the corpus luteum hormone. After spontaneous termination of pregnancy or instrumental delivery, such menstrual disturbances as hypomenorrheas and amenorrheas may be due solely to local, mechanical traumatization of tissues. Traumatization by a sharp curette affects the uterus itself, and most frequently the region of the internal os. Pathologico-anatomic studies of Stieve disclosed that the cervix may acquire a structure resembling that of cavernous bodies, the connective tissue becomes friable, the muscular elements and the glands proliferate, and the venous system develops. It appears that even a relatively small obstacle may prevent the natural flow of fluid contents from the uterine cavity.

Reporting 22 cases, the author states that instrumental damage leads to the formation of adhesions and scar tissue in the cervical canal, and often results in stenosis or even atresia of the canal. In all patients with hypomenorrhea and amenorrhea, developing soon after artificial abortion and delivery with operative interference, it is necessary to see whether a uterine sound can be passed through the cervical canal. In recent cases it is sufficient to dilate the cervical canal once with Hegar dilators up to No. 7. In neglected cases repeated dilatation is required. In some instances it is necessary to excise the obstacle and then follow with repeated dilatations. Neglected cases require also hormonal therapy.

ALEXANDER GABRIELIANZ.

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*Details of technic.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

Meeting of May 12, 1936

The following papers were presented:

Comparative Study of Pelvic Temperatures Under Various Therapeutic Procedures. Dr. Harold C. Ingraham. (For original article, see page 1048.)

A Review of 226 Cases of Obstetric Analgesia. Dr. Virgil G. Damon (by invitation). (For original article, see page 1009.)

Therapeutic Abortion by Means of X-ray. Drs. Max D. Mayer, William Harris, and Seymour Wimpfheimer. (For original article, see page 945)

CHICAGO GYNECOLOGICAL SOCIETY

Meeting of March 20, 1936

The following case reports and papers were presented:

Two Cases of Unruptured Ectopic Pregnancy. Dr. Milton M. Scheffler. (For original article, see page 1061.)

Hemorrhage Into a Fibroid During Pregnancy. Dr. Wm. H. Browne.

A Biologic Test for the Diagnosis of Intrauterine Fetal Death. Dr. George H. Rezek. (For original article, see page 976.)

The Surgical Treatment of Puerperal Sepsis. Dr. A. F. Lash.

A Critical Study of the Low Cervical and Classical Cesarean Section Operation. Dr. Frederick H. Falls. (For original article, see page 989.)

BROOKLYN GYNECOLOGICAL SOCIETY

Meeting of March 6, 1936

The following paper and case report were presented:

Carcinoma of the Body of the Uterus. Dr. C. C. Norris and Dr. F. S. Dunne. (For original article, see page 982.)

A Full-Term Pregnancy Complicated by an Acute Intestinal Obstruction and False Labor Pains. Dr. John Casagrande. (For original article, see page 1058.)

Department of Reviews and Abstracts

Selected Abstracts

Pathology of Labor

Brown, R. Christie: **The Treatment of Obstetric Disproportion,** Brit. M. J. **1:** 1251, 1935.

Recognition of the presence of disproportion is difficult, yet most important. Major disproportions are easily recognized by the ordinary methods of measurement, which reveal marked pelvic contraction. They all require cesarean section. In cases of minor disproportion the x-ray offers an additional aid to diagnosis, but the outcome of labor in these cases is uncertain, and a decision can be made only after a test of labor. This applies especially to primiparas. Pelvic measurements alone are not a criterion; they must be considered in conjunction with all other factors when giving the prognosis, i.e., the size of the fetal head, general build of the patient, age of the patient, mobility of pelvic joints, presentation, course of first stage, force of uterine contractions, fortitude of the patient, and the molding of the head.

A vaginal examination is advocated in every case during pregnancy and after membranes rupture during a test of labor. Induction of premature labor for disproportion has no place in the delivery of a primipara, but it may be useful in the delivery of a multipara whose record of a former labor has been carefully kept and can be used as a guide to the ability of the patient to deliver herself. In minor disproportions only a test of labor will estimate the patient's chances for delivery which no amount of skill can lead an observer to decide upon during pregnancy. In all cases of doubt, in the primipara, the patient should be allowed to go into labor spontaneously at term and the labor be observed. In this way an accurate opinion can be arrived at during the first stage.

F. L. ADAIR AND S. A. PEARL.

Pettit, Garland, Dunn, and Shumaker: **Correlation Between the Shape of the Female Pelvis and the Clinical Course of Labor,** Western J. Surg. Obst. & Gynec. **44:** 1, 1936.

Applying the roentgenologic technic and the classification of pelves elaborated by Caldwell and Moloy in a series of 100 consecutive labors, the authors conclude that the classification of pelves on an architectural basis by roentgen methods is a simple and clinically feasible procedure, and that in a significant number of cases a difficult labor can be forecast by pelviography in patients whose obstetric measurements by ordinary methods appear normal. This is especially evident in the android group.

HUGO EHRENFEST.

Mann, John: The Mechanism of Rotation in Occipito-Posterior Positions, Canad.
M. A. J. 33: 607, 1935.

The author reviews and discusses various factors concerned with the mechanism
of rotation in occipitoposterior positions. Mention is made of the size and shape
of the maternal pelvis in relation to the maximum available diameters, and the
usual theories are discussed. Positions and degrees of flexion of fetal heads are
used to explain failures of rotation. The idea is advanced that the fetus himself
is responsible for some rotation of his head. Analgesic drugs that do not inter-
fere with the force of uterine contractions are satisfactory and may be used lib-
erally. In prolonged first stage, membranes should remain intact but after com-
plete dilatation they should be ruptured.

A general discussion of various treatments follows, after which the author de-
scribes his universal joint forceps and their use. He does not present any data
or statistics.

H. CLOSE HESSELTINE.

te Groen, L. J.: Vertex Presentation With Extended Head, South African M. J.
9: 305, 1935.

Two causes for this condition are offered: the large, wide pelvis and the flat
pelvis. The term ''sincipital presentation'' is adopted. In South Africa it is
seen most commonly in women with large, wide pelves, and where the baby has a
round head.

The mechanism of the development of the attitude is described. A round fetal
head and a wide pelvis with little resistance lead to this attitude in multiparas when
the head is high above the brim and begins to enter the pelvis only when labor is
well advanced, and where the membranes had ruptured with early pains.

Posture of the patient is given as a factor in influencing presentation. The
author believes that where the baby's back is on the right and the patient lies on
her left side, the descent of the head will encourage sincipital or even brow or face
presentations. Amsterdam teaches to allow the patient to remain on the same side
as the back of the baby in normal pelves, and on the opposite side in cases of flat
pelvis.

In sincipital presentations the large fontanel is readily felt. The mechanism
of labor is akin to that of a brow presentation, except that in the latter the maxillary
fossae engage under the symphysis, whereas in the sincipital form the root of the
nose is under the symphysis.

F. L. ADAIR AND S. A. PEARL.

Kawakami, H.: Application of ''Atonin'' in the Clinic, Jap. J. Obst. & Gynec.
17: 326, 1934.

The Japanese preparation of pituitary extract is known as ''atonin.'' Ka-
wakami used this drug in about 200 patients during every stage of labor. In the
first stage of labor he injected varying doses up to 0.5 c.c. However, he suggests
that not more than 0.3 c.c. be used during labor. He found that atonin was fol-
lowed by such complications as: rupture of the perineum, fetal asphyxia, and
cerebral hematoma. There were more of such complications among patients who
received atonin than among those who did not. Furthermore, the complications
were proportional to the dose used. The higher the dose the more frequent the com-
plications. The author found the drug very useful for postpartum hemorrhage. He
prefers subcutaneous injection to the intravenous use.

J. P. GREENHILL.

Riley, P. W. S.: **Obstructed Labour,** New Zealand M. J. 34: 119, 1935.

A case of obstructed labor due to a pelvic kidney is reported. True nature of case was revealed only at operation. A unilateral, lobulated, single kidney was lying in the true pelvis and to the right. No kidney was palpable on either side of the lumbar region. Pyelogram confirmed the singularity of the organ. It was a congenitally misplaced kidney, said to be more common in women. Patient had no structural genital defects or leakage of urine indicating an aberrant ureter.

F. L. ADAIR AND S. A. PEARL.

Katsu, Y.: **A Newly Discovered Symptom for the Diagnosis of Anencephalus,** Jap. J. Obst. & Gynec. 15: 507, 1932.

Usually the diagnosis of anencephalus is made before delivery on the following vaginal findings: (1) palpation of spongy soft tissue surrounded by projecting cranial bones, (2) abnormal protrusion of the eyeballs, (3) palpation of bony protuberances such as the sella turcica or the foramen magnum, (4) abnormally small head, and (5) difficulty in obtaining ballottement due to an abnormally short neck. In addition to these findings the x-ray examination supplies confirmatory evidence as does also Negri's sign. According to the latter sign, if pressure is made on the cerebral substance at the base of the skull, the fetus responds with a violent motion or with spasmodic movements. The author in two cases found that pressure on the cerebral substance also produced a sudden and definite slowing of the fetal heart rate. Release of the pressure resulted in a normal heart rate.

J. P. GREENHILL.

Ahltorp, G.: **A Contribution to the Diagnosis of Anencephalus Before Delivery,** Acta obst. et gynec. Scandinav. 13: 93, 1933.

Ahltorp describes a case of anencephalus in which the diagnosis was made before delivery. The diagnosis was based chiefly on the circumstance that the fetal movements were especially lively at every rectal palpation on the presenting head of the fetus. This symptom, first described by Laulaigne, seems to have been subsequently overlooked as an indication of anencephalus. The diagnosis was verified by x-ray examination.

An unmistakable diagnosis can be obtained by radiography. This has been done in more than 40 cases up to the present time.

X-ray examination to ascertain the possible presence of an anencephalus is indicated under the following conditions: (1) when the fetal head cannot be surely palpated; (2) in hydramnion, with the possibility of twins excluded; (3) when there are vigorous fetal movements during palpation of the suspected presenting part.

J. P. GREENHILL.

Porcardo, Diago: **A Sign of Orientation in the Diagnosis of Anencephalus,** Ginecologia (Torino) 1: 845, 1935.

The author calls attention to a sign easy to verify in the anencephalus. It consists in the rapid movements of the presenting part (face presentation), but particularly of the mouth to the point of squeezing the finger introduced in it.

AUGUST F. DARO.

Laubscher, A. E.: **Methods of Terminating Labor,** South African M. J. 9: 222, 1935.

An outline of the physiology and mechanism of the onset of normal labor is presented, which is summarized as ''a number of stimulants with cumulative effect

are brought to act on a suitably prepared uterus and thereby influence the uterus in such a way that it starts contracting rhythmically. . . . Pressure of the presenting part on the lower uterine segment plays its part in the determination of the frequency and severity of the pains.''

Methods advocated are dilatation of cervix and blunt curette in the early months, using great caution not to perforate uterus. In later months, between third and seventh, vaginal hysterotomy is advised for skilled operators. After the seventh month induction is by drugs: castor oil, quinine, and pituitrin.

Rupturing the membranes is a dangerous procedure. The author alludes to the use of the stomach tube in the uterus and to the use of the metrorynter; the latter is more certain of producing dilatation.

<div align="right">F. L. ADAIR AND S. A. PEARL.</div>

Stacey, J. Eric: Analgesics in Labour, Brit. M. J. 1: 817, 1935.

The author approaches the subject of analgesia in labor from the standpoint of relief of pain for the whole of labor. So little is known of the mechanism of pain that he feels we have no scientific basis for relieving its symptoms. An impoverished blood supply to muscles will elicit pain due to a local production of a chemical material called ''p'' substance. For practical purposes the author feels that a proper attitude toward labor on the part of the mother and confidence in her accoucheur are the most important factors in the relief of pain. Next, the choice of drug or anesthetic is of prime importance.

For the first stage he has great success with chloral (30 or 40 gr.) with or without potassium bromide in 4 or 6 ounces of water or glucose. This is repeated in one hour. It tides the patient over to the period when morphine may be safely given. Hyoscine used with morphine, he feels, needs a constant attendant.

He gives 1/100 gr. of hyoscine repeated in three-fourths hour, two hours later, and again three hours later depending on the reaction on the patient. In primiparas he starts this treatment when the cervix is taken up and the os is from 3 fingers to ½ dilated, and the pains are ten minutes or less apart and of fifteen to thirty seconds' duration.

He enumerates the advantages of hyoscine as (1) simple of administration, (2) rarely produces hyperexcitability, (3) it produces forgetfulness of pain, (4) it does not cause uterine contractions to decrease, (5) the infant does not suffer from oligopnea, (6) the third stage is not prolonged, (7) postpartum hemorrhage is nil. Morphine he considers one of the most, if not the most, valuable analgesic in labor.

Of other analgesics he found Gwathmey's methods tedious and not always effective. He has not had much experience with the barbiturates except nembutal which produced pallor and coma in one or two patients and alarmed him. The author finds no better analgesic in the second stage than chloroform, or gas and oxygen. He thinks chloroform safe and uses it routinely. He uses gas in selected cases.

<div align="right">F. L. ADAIR AND L. G. COON.</div>

Wachenfeldt, S.: Studies on Deliveries Among Multiparas, Acta obst. et gynec. Scandinav. 15: 1, 1935.

In the Woman's Clinic at the University of Lund from 1911 to 1930, there were observed 11,990 pregnancies which resulted in the birth of children weighing 2,500 gm. or more, in multiparous women. The duration of labor averaged about ten hours. It was shortest in women who had had 2 or 3 children but rose with further increase in parity. The frequency of head presentations diminished with increase in parity, whereas transverse presentations tended to rise in frequency

with increase in parity. Breech presentations occurred with equal frequency among all the patients. As parity increased the weight of the children of both sexes increased.

Placenta previa increased with increase in parity. There did not seem to be any change in the incidence of the toxemias of pregnancy. There was, however, a greater predisposition to preeclampsia and eclampsia as the age of the patient increased. Abruptio placentae definitely increased with increase in parity as did also diseases accidental to pregnancy. Postpartum hemorrhage increased in frequency with increase in parity, but puerperal infection tended to decrease in frequency.

There was no difference in mortality between the primiparas and multiparas, but the death rate of the children showed a marked rise among the multiparas.

<div style="text-align:right">J. P. Greenhill.</div>

Healy, T. M.: Observations on the Results of Operative and Spontaneous Deliveries, Irish J. M. Sc. **6:** 543, 1934.

An increasing incidence of operative interference during pregnancy and labor is revealed in the publications from almost all maternity centers. The obstetrician of today, working in a well-equipped hospital as a member of a team, rejoices in the knowledge that he can show better statistics in his operative cases than were obtained when surgical intervention during parturition first became fashionable. Whether he has fewer fatalities to his discredit after a decade or two in practice, is more open to doubt; for in his enthusiasm for manual dexterity he is in danger of losing sight of the fact that he has yet to achieve results which will bear comparison with those of the spontaneous deliveries he so frequently cuts short. If we justify our operations by pleading that modern civilization has produced women who cannot deliver their babies, it seems arrogant to assert that the same generation has begotten a race of obstetricians to make good the failures.

<div style="text-align:right">Wm. C. Henske.</div>

Hirst, J. C.: Active Versus Conservative Management of Planned Deliveries, Am. J. M. Sc. **190:** 806, 1935.

Conservative ward obstetrics is safest for mother and child; but reasonable assistance by a trained specialist yields as good results with more relief. Internes should be preinstructed in proper methods of delivery and the importance of rigid adherence to technic, and must be supervised in every abnormal labor and in all operative deliveries. A member of the major obstetric staff should be present at all operative deliveries other than outlet forceps, and at all breech deliveries. No effort whatever should be made to interfere with natural birth for the purpose of exhibition to students, since demonstration forceps or other operative deliveries instituted only for instruction of students or internes have been found unjustifiable.

<div style="text-align:right">J. Thornwell Witherspoon.</div>

Robiolis: Reflections on the Delmas Procedure, Bull. soc. d'obst. et de gynéc. **24:** 582, 1935.

After having performed the Delmas method of forcible dilatation of the cervix under spinal anesthesia twelve times, the author stopped to analyze his results. The first patient died four hours after labor but the baby remained alive. The second patient was in a precarious condition for three hours after delivery. The same held true for the third patient who had an extensive postpartum hemorrhage. The fourth patient suffered an extensive hemorrhage from the left side of the

vagina and the cervix. The fifth and sixth cases had no complications. The seventh patient had repeated hemorrhages which finally necessitated a vaginal hysterectomy. The eighth patient had a severe laceration of the cervix. The ninth patient died, three hours after delivery of a dead baby, without any signs of hemorrhage. The tenth patient suffered from severe headaches. The eleventh patient had a serious cervical laceration. The twelfth patient was critically ill for eight hours after delivery and had to be transfused although there was no hemorrhage. On the basis of this experience the author feels that the Delmas procedure should be used only in rare cases when it is impossible to deliver a baby by any other means. It should be performed only in a hospital where preparations should be at hand for possible complications. The patient must be closely watched for at least five to six hours after delivery.

<div align="right">J. P. GREENHILL.</div>

Rucker, M. Pierce: Obstetrical Shock, Virginia M. Monthly 62: 254, 1935.

Obstetric shock may be divided into three groups: (a) that due to hemorrhage; (b) other conditions well recognized as causing shock that may be concomitant with labor such as ruptured appendix, perforating gastric ulcer, ovarian cysts with twisted pedicle, etc., and (c) shock with no discoverable cause. The author quotes 15 instances of obstetric shock with no discoverable cause in a series of 7,177 cases of abortions and full-term labors. He suggests as possible cause of this type of shock the spill of blood or fluid into the peritoneal cavity through the fallopian tubes. It seems noteworthy that among the 15 cases reported by him there was only one of unaided delivery.

<div align="right">EUGENE S. AUER.</div>

Wahl, F. A.: Sequelae in Children Born After Tribrom-Ethanol (Avertin) Anesthesia, Arch. f. Gynäk. 157: 17, 1934.

The use of tribrom-ethanol is of serious consequence to the babies that are born under the influence of this drug. Over 50 per cent show marked asphyxia even hours after delivery. In addition, over one-half are markedly apathetic, have a weakened cry, or rather whimper, nurse very poorly, and therefore have a marked increase in frequency and amount of aspirations and show a disturbed weight curve. From the fetal point of view, therefore, this method of anesthesia should be vigorously condemned.

<div align="right">RALPH A. REIS.</div>

Atlee, H. B.: Evidence in Favour of a More Active Puerperium: A Study of 500 Cases, Canad. M. A. J. 33: 144, 1935.

In a study of the results of physical activity in the puerperium, the author finds some evidences to refute the more common idea that the puerperal woman should be inactive.

On the day following delivery the patient sits up in bed, but when reclining should be on her sides and abdomen. The leg, arm, and body exercises are gradually instituted beginning on the second day. On the fourth day the patient sits in a chair by the side of the bed. These activities are reserved for the normal cases and those having had forceps delivery and perineal repairs. If the patient objects, she is not forced, and if a fever develops she is restricted to bed rest.

The tables indicate that with a more active puerperium involution is not impaired, prolapse is not increased, the lochia disappear more quickly, infections

and embolisms are not increased, and the patients are able to take up their household duties earlier and with more zest. However, this series consists of only 500 cases.

<div align="right">H. CLOSE HESSELTINE.</div>

Moir, Chassar: The Merits and Demerits of Oxytocic Drugs in the Postpartum Period, Proc. Roy. Soc. Med. 28: 1654, 1935.

Oxytocic substances are administered during the puerperium for three reasons: (1) To prevent atonic hemorrhage, (2) to check uterine hemorrhage, and (3) to promote involution.

As far as the writer knows there is no direct evidence that *involution* is aided by such drugs. Stopping indiscriminate routine use of these drugs in his services, in his belief, has saved nurses much unnecessary work, patients much inconvenience and nausea, the hospital a good sum of money, and as far as could be seen the uteri involved just as they had done before. Misuse of ergot may lead to *gangrene* of the extremities. The *effect of oxytocic drugs* can be recorded either by the Bourne and Burn's method (water filled bag in uterus connected with manometer) or Dodek's instrument recording changes in uterine shape through abdominal walls. In his own studies the writer found the latter method entirely sufficient for the purpose.

Glycerin, injected into uterus through a catheter, is an unreliable method of stimulating uterine contractions. *Gravitol,* a proprietary drug claimed to have ergot-like action, injected intramuscularly has a relatively feeble effect for about twenty minutes. *Histamine* (on the market under the trade name ''ergamine'') cannot be given in a dose large enough to be therapeutically effective without also producing undesirable by-effects. It is unsuited for any obstetric emergency. *Ergotoxine* and the almost identical alkaloid *ergotamine* (trade names femergin or gynergen) are now freely used. Other ergot alkaloids more recently isolated are *sensibamine* and *ergoclavine.* All four make a well-defined group in regard to their clinical action which is practically the same. They have large molecules and, perhaps because of this, are slow to take effect when administered in permissible dosage. When given by mouth no effect is seen in graphic recording before thirty-five minutes have elapsed. Resulting uterine contractions are small and erratic. It seems possible that repeated oral administrations may lead to a prolonged heightened irritability of the uterus. Administration of members of this group by intramuscular injection is a more satisfactory procedure. After about twenty minutes strong contractions gradually set in which soon merge into a uterine spasm, followed by strong isolated contractions for several hours. The new alkaloid *ergometrine* in several respects contrasts to those already mentioned. Clinically and pharmacologically it must be placed in a class by itself. It is remarkable for its rapidity of action. It works by mouth usually in five to eight minutes, by intramuscular injection in three to four and a half minutes, by intravenous administration in about one minute. There is a uterine spasm which lasts for about an hour and is followed by strong regular contractions for one and a half to three hours. Clinically the ergotoxine-ergotamine group is distinctly inferior to ergometrine, though the spasm of the first group, setting in later, lasts longer.

There follows a consideration particularly of posterior pituitary extracts in the prophylaxis of postpartum hemorrhage. The purified pitocin, largely freed of the pressor principle, is preferable to the usual preparations especially in cases of obstetric shock. Pituitary extract for long has been the sheet anchor in treating postpartum hemorrhage on account of its rapid and intense action, but the new ergometrine now is a serious rival, especially when administered intravenously. Its use is not contraindicated by obstetric shock.

<div align="right">HUGO EHRENFEST.</div>

Naljawinsky, W.: Uterine Ruptures, Monatschr. f. Geburtsh. u. Gynäk. **98:** 167, 1934.

Among 6,367 labor cases at the Second Moscow Woman's Clinic, there were 15 cases of uterine rupture. One of these women had a rupture of the uterus twice. The author found that rupture of the uterus occurred much more frequently in multiparas than in primiparas. Symptoms of rupture may be entirely absent. The progress of labor may not cease after the rupture has occurred, and in some cases spontaneous delivery took place after the rupture. In the diagnosis of uterine rupture the history and external examination are of the greatest importance. The most efficient treatment for uterine rupture is an abdominal operation. Etiologic factors in uterine rupture are connective tissue changes in the uterus, especially the presence of scars and inflammatory changes.

<div align="right">J. P. GREENHILL.</div>

Bazán, Julio, and Imaz, Francisco A. Uranga: The Treatment of Rupture of the Uterus, Rev. españ. de obstet. y ginec. **20:** 454, 1935.

The writers report 21 cases of rupture of the uterus in 27,500 obstetric patients admitted to the hospital. Fourteen patients were cured and 7 died, 2 from peritonitis and 5 from hemorrhage and shock. Surgery was performed in 18 patients while three patients were treated conservatively. Hysterectomy was done in 13 cases and 2 cases were sutured. Two of the hysterectomies were done vaginally and one case was sutured from below. Of the 13 abdominal hysterectomies, 7 patients lived and 6 died of either hemorrhage, shock, or peritonitis. All patients operated upon vaginally lived. Patients' ages ranged from twenty-two to thirty-five years. All except three of the patients were multiparas with many children. Blood transfusions were done in only 9 patients, 7 of whom lived. The small number of transfusions was due to the fact that during the first few years of existence of the hospital, the blood transfusion department was not functioning. The writers agree that surgery and not expectant treatment should be the procedure to follow but that the patient must be prepared by transfusion, especially when there is shock—even if the operation must be delayed for a few hours. Suturing the uterus may be done in clean cases.

<div align="right">F. L. ADAIR AND J. SUAREZ.</div>

Coutts, D.: Foetus Removed From Mother's Thigh Following Rupture of the Uterus, Proc. Roy. Soc. Med. **29:** 308, 1936.

Under this striking title the following case is reported: A Hindu woman, thirty-five years old, was admitted to the Hospital for Women in Patna, India. A few hours previously she had been knocked down and run over by a heavy motorbus.

Outside of cuts and bruises on various parts of the body she showed enlargement of the lower abdomen and a swelling in the upper third of the right thigh. The latter swelling on palpation suggested the presence of fetal parts, and on questioning, it was ascertained that the woman had not menstruated for the last four months. Vaginal examination revealed an enlarged and soft uterus, tilted to the right. Cervix enlarged, soft, closed, no bleeding. To right extreme tenderness. Catheter urine clear. Pulse 86, small, easily compressible; respiration 37. Patient in profound shock and semiconscious. Appropriate measures against shock immediately taken. Next day patient was improved and swelling in thigh larger. An x-ray picture (presented in this report) confirmed palpatory findings, namely, a fetus with head down, lying in front of femur. With a vertical incision, extending up to the groin, the fetus was removed, lying just under skin and superficial fat in a bag of bloody fluid. The inguinal ligament was found detached at both its ends and the muscles attached to the anterior third of the right iliac crest were torn. Then incision was extended upward, following the cord, until the uterus was reached.

There was a rupture anteriorly, grasping the placenta which was extracted. Practically no bleeding. The structures below the deep fascia of the thigh were unaffected. Some blood in peritoneal cavity. Considering the patient in no condition for a hysterectomy, the uterine rent was stitched up like in a cesarean section. Within the abdomen a big rent, eight inches long, was felt running up to the costal arch. It was closed, after further lengthening the incision. Finally wound closed and two drainage tubes inserted through stab wounds. Recovery proceeded rather satisfactorily when patient, about five weeks after operation, on account of a terrific earthquake rushed outside in a heavy rain. She developed a pneumonia from which she recovered, finally was discharged in satisfactory condition.

The striking displacement of the fetus could be explained in two ways: (1) Bus struck her on the left, running over her, rupturing uterus and forcing fetus down into thigh; (2) blow and pressure were on the right, stripping skin and fascia off the thigh, they detached the inguinal ligament and abdominal muscles, tore the peritoneum and ruptured the uterus. On rebound, the contracting uterus squeezed the fetus under the skin of the right thigh along the line of least resistance.

<div align="right">HUGO EHRENFEST.</div>

Frewer, Edward: Twins With Doubly Knotted Cords, Brit. M. J. 1: 159, 1936.

A case is reported of twins sharing one amniotic sac and showing an unusual development of the umbilical cords. Arising from the placenta was a single thick cord; 1½ inches from the placenta it divided into 2 cords, one unusually thin, 25 inches long, belonging to the first child, the other of normal thickness 15 inches long. The thin and longer cord formed two knots by being looped and twisted about the thicker, shorter cord. Both knots were easily loosened, and no adhesions were present. The babies weighed 3 pounds 10 ounces and 4 pounds 5 ounces, respectively. The smaller of the two survived; the larger died after thirty hours with signs of cerebral immaturity.

<div align="right">F. L. ADAIR AND S. A. PEARL.</div>

Coleman, J. Stanley: Two Cases of Twin-Locking, Lancet 1: 196, 1936.

Because twin-locking is so very rare, the author reports two cases of this condition.

The first patient was aged twenty-nine, gravida ii. After 28½ hours of labor, the cervix was still three-fourths dilated. Under anesthesia it was fully dilated and above were two heads palpated, impacted at the brim. The second head was wedged under the chin, against the neck and upper thorax of the first fetus. The second head was liberated and displaced upward. The head of the first fetus was flexed, rotated and then delivered by forceps. Loops of cord were then discovered to be responsible for the extension. Because of moderate bleeding the second fetus was immediately delivered by forceps. The twins were binovular. The mother and twins had an uneventful recovery.

The second patient was aged twenty-seven, a primigravida, and was admitted to the hospital because of severe toxemia. The toxemia improved. Nineteen days after hospitalization the membranes ruptured spontaneously and labor ensued. After eighteen hours it was evident that a serious obstruction existed. An examination under anesthesia revealed a prolapse of a hand under the chin of the first fetus and the head of the second fetus was at the inlet. The second head was displaced and the first head was delivered by forceps. The second twin was delivered by forceps immediately.

In both of these patients the anesthesia and manipulations were carried out with the patient in the left lateral position. The author advises early interference before impactions become severe.

<div align="right">H. CLOSE HESSELTINE.</div>

Constantine, M. C. E.: A Case of Quadruplets, Brit. M. J. 2: 1206, 1935.

Quadruplet pregnancy occurs once in 654,455 births, as calculated by Diddle and Burford from a total of 219,899,446 recorded births.

The author describes the case of a para iii, aged thirty-four, giving birth to four living boys, diagnosed antenatally by x-ray. The delivery was uneventful. Two babies presented as vertex and two by the breech.

The placenta was expelled in two portions. One larger mass consisted of two placentas joined by contiguous margins. One of these had one chorionic and two amniotic sacs; the attached one had a distinct chorion and amnion. The placenta, expelled separately, had a complete chorion and amnion. Hemorrhage was not excessive.

The infants weighed 3 pounds 7½ ounces, 2 pounds 2½ ounces, 3 pounds 8½ ounces, and 3 pounds 10 ounces twelve hours after birth. First born died three days later as result of atelectasis of lungs and a patent foramen ovale. The second baby died on the sixth day, showing atelectasis at postmortem. The mother's puerperium was normal.

F. L. ADAIR AND S. A. PEARL.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, March 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in Atlantic City, N. J., on June 8 and 9, 1937, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled date of examination.

Central Association of Obstetrics and Gynecology

The Eighth Annual Meeting of The Central Association of Obstetricians and Gynecologists was held in Detroit, October 15, 16, and 17. The guest speaker was Dr. Emil Novak of Baltimore. The following officers were elected for the coming year:

President: Dr. Jean Paul Pratt, Detroit.
President-Elect: Dr. Robert D. Mussey, Rochester.
Vice-President: Dr. Calvin R. Hannah, Dallas.
Secretary-Treasurer: Dr. Ralph A. Reis, Chicago.
Asst. Secretary: Dr. William F. Mengert, Iowa City.
Dallas was chosen as the meeting place for 1937.

Correspondence

To the Editor:

In line with our interest in "medical aspects of human fertility," we are impressed by the extensive and increasing interest in and reliance upon the so-called "safe period" as a means of contraception. There is urgent need for determining, as accurately as possible, whether there exists, for the regularly menstruating woman, a predictable and reliable moiety of her cycle in which fertilization is impossible. The National Committee on Maternal Health is undertaking to collect pertinent data which, by reason of their source, will be of exceptional value. The cooperation of the medical profession is invited for this investigation.

We seek to enlist specially qualified married couples who will scrupulously keep and transmit to us—through their doctors and, of course, confidentially—accurate and complete records of menstruation and coitus over a long period of time, several years if possible. We hope that physicians reading this journal may, directly or indirectly, enable us to receive the cooperation of suitable couples, of whom one or both are, say, physicians or graduate students or faculty members or research workers in biologic or other scientific departments, therefore competent to furnish trustworthy records and also scientifically interested in contributing to this investigation.

A couple such as we wish to enlist might prefer not to have a pregnancy develop during the next year or more, although if one did develop it would not be calamitous. Accordingly the couple would observe the so-called "safe period" as their sole means of avoiding conception. If that succeeds, and then the time comes when they desire a child, they would reverse their practice, confining coitus to occasions outside the "safe period," or they would at least restrict intercourse to the moities of the menstrual cycle when, theoretically, pregnancy is most likely to result, and then record how soon it does result. Needless to say, there must be no known or probable factor of involuntary sterility in either one of the couple.

The frankly experimental character of the coital practices upon which these records are based, and the special qualifications of the recorders, will make these data uniquely valuable.

The Committee is peculiarly fitted to collect these records. Its territory is large enough to encompass couples in number adequate for the investigation—couples who, by reason of their particular qualifications and their willingness to volunteer, must be few in any one community, no matter how large the latter may be.

Upon application, we shall be glad to furnish to physicians simple record forms and brief instructions easy to follow which they may distribute to cooperating patients. We hope to hear from as many as possible who are reached by this announcement. Please address: National Committee on Maternal Health, Inc., New York Academy of Medicine Building, 2 East 103rd Street, New York, N. Y.

—RAYMOND SQUIER, M.D.
Executive Secretary.

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